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Performance of Comorbidity Adjustment Measures to Predict Healthcare Utilization and Expenditures for Patients with Diabetes Using a Large Administrative Database

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Abstract

Performance of Comorbidity Adjustment Measures to Predict Healthcare Utilization and Expenditures for Patients with Diabetes Using a Large Administrative Database

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Objective: The objective of this study was to compare the use of different comorbidity measures to predict future healthcare utilization and expenditures for diabetic patients. **Methods:** This was a retrospective study that included 8,704 diabetic patients enrolled continuously for three years in the Department of Defense TRICARE program. Administrative claims data were used to calculate six comorbidity measures: number of distinct medications, index-year healthcare expenditures, two versions of the Charlson Comorbidity Index (CCI), and two versions of the Chronic Disease Score (CDS). Linear regression models were used to estimate three health outcomes for one- and two-year post-index periods: healthcare expenditures (COST), number of hospitalizations (HOS), and number of emergency department visits (ED). Logistic

regression models were used to estimate binary outcomes (above or below the 90th percentile of COST; ≥ 1 HOS or none; ≥ 1 ED or none). Comparisons were based on adjusted R^2, areas under the receiver-operator-curve (*c* statistics), and the Hosmer-Lemeshow goodness-of-fit tests. **Results:** The study population had a mean age of 51.0 years (SD = 10.5), and 46.3 percent were male. After adjusting for age and sex, the updated CCI was the best predictor of one-year and two-year HOS (adjusted R^2 = 8.1%, 9.3%), the number of distinct medications was superior in predicting one-year and two-year ED (adjusted R^2 = 9.9%, 12.4%), and the index-year healthcare expenditures explained the most variance in one-year and two-year COST (adjusted R^2 = 35.6%, 31.6%). In logistic regressions, the number of distinct medications was the best predictor of one-year and two-year risks of emergency department use (*c* = 0.653, 0.654), but the index-year healthcare expenditures performed the best in predicting one-year and two-year risks of hospitalizations (*c* = 0.684, 0.676) and high-expenditure cases (*c* = 0.810, 0.823). The updated CCI consistently outperformed the original CCI in predicting the outcomes of interest. **Conclusions:** In a diabetic population under age 65, the number of distinct medications and baseline healthcare expenditures appeared to have superior or similar powers compared to the CCI or CDS for the prediction of future healthcare utilization and expenditures. The updated CCI was a better predictor than the original CCI in this population.

Table of Contents

List of Tables

List of Figures

Chapter 1 Background

1.1 Introduction

Comorbidity adjustment measures are used frequently in health services and epidemiological research to compare patient health status or to control for confounding effects. The primary objective of this study is to compare the utility of two comorbidity adjustment measures, the Charlson Comorbidity Index and the Chronic Disease Score, in terms of their predictive power and accuracy for several health outcomes. These outcomes include one-year and two-year total healthcare expenditures, number of hospitalizations, and number of emergency department visits. Patients with diabetes enrolled in the Department of Defense TRICARE insurance program were used as the study population because diabetic patients tend to suffer from multiple chronic conditions in addition to diabetes.

The following sections will discuss comorbidity, diabetes, the Department of Defense TRICARE program, study rationale, study objectives, and research hypotheses.

1.2 Comorbidity

Risk is a multifaceted construct that is as complex as it is abstract, yet ubiquitous in everyday life. In medical research, such risks could include potential side effects from prescription medications or serious adverse reactions to vaccines. Some risks are

measurable, such as age and sex, while others could not be evaluated as easily, such as the perception of control over one's health status. Many attempts have been made to identify risk factors, variables associated with increased risks of certain diseases or conditions, which may be used to estimate the level of risk in an individual or a group of people. For example, elevated serum cholesterol level has long been recognized as a risk factor for coronary heart disease.[1]

Iezzoni identified demographic characteristics, clinical factors (including comorbidity), socioeconomic factors, health-related behaviors, and patient attitudes as the most important risk factors in health services research.[2] Among this large array of risk factors, comorbidity is one that has become increasingly popular in estimating a person's health status, and much research has been conducted to measure comorbidity as well as to refine these measures.

1.2.1 Definition of Comorbidity

Comorbidities are "diseases unrelated in etiology or causality to the principal diagnosis."[3] Despite their textual similarities, comorbidity is different from "multimorbidity" and "complications" in their connotations. Conceptually, comorbidities are etiologically unrelated to the principal diagnosis and are established only after the principal diagnosis is established. On the other hand, multimorbidity refers to the

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1 William B. Kannel et al., "Factors of Risk in the Development of Coroniary Heart Disease - Six-Year Follow-up Experience: The Framingham Study," *Annals of Internal Medicine* 55, no. 1 (1961).

2 Lisa I. Iezzoni, "Range of Risk Factors," in *Risk Adjustment for Measuring Health Care Outcomes*, ed. Lisa I. Iezzoni (Chicago, Ill: Health Administration Press, 2003).

3 Ibid.

coexistence of multiple diseases in a patient, without defining an index disease or a primary diagnosis.

The distinction between comorbidities and complications is not as conspicuous and unambiguous, as interpretations of the same clinical manifestation may vary under different circumstances. For example, blindness is regarded as a serious complication associated with poor glycemic control in diabetic patients, but it could also be viewed as a comorbidity instead of a complication if other diseases such as cataracts or glaucoma cause the blindness in a patient with diabetes. Nevertheless, in general, comorbidities should be distinguished from complications: while comorbidities are not etiologically related to the principal diagnosis, complications are usually unfavorable medical conditions resulting from the principal diagnosis.

1.2.2 Reasons to Measure Comorbidity

Measuring comorbidities is important for several reasons. In the clinical setting, the focus of care tends to center on a patient's principal diagnosis, be it acute or chronic. Medications, diagnostic tests, and functional assessments are usually planned based on the symptoms presented by the patient and the diagnosis thus made. Yet, oftentimes healthcare providers encounter patients who have more than one clinical condition that deserves medication attention, and comorbidities may influence how a clinical decision is made or how a treatment plan is devised. For example, while calcium channel blockers are recommended for hypertensive patients with comorbid diabetes, the same drug class

is not recommended for patients with both hypertension and chronic kidney disease.[4] Whether and when a drug therapy should be initiated may depend on a patient's comorbid conditions: hypertensive patients who have a diagnosis of heart failure should start drug therapy earlier than those who do not.[5] Treatment goals may also vary due to differences in patients' comorbidities.[6]

The second reason to measure comorbidities is that they could serve as predictors of health outcomes, such as hospitalizations or emergency department visits. Intuitively, patients who have more comorbidities should be sicker than those with fewer or no comorbidities. Indeed, the number of comorbid conditions is correlated with the volume of health services utilization: patients who have more comorbidities tend to seek more services from primary care physicians and specialists and are more likely to be admitted into hospitals.[7] Comorbidity is important in determining healthcare costs of patients.[8] Studies have shown that classification of patients is possible based on their healthcare costs and comorbidities.[9,10] Identifying the subgroup of patients who utilize more

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4 Aram V. Chobanian et al., "The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 Report," *Journal of the American Medical Association* 289, no. 19 (2003).

5 Ibid.

6 David M. Nathan et al., "Medical Management of Hyperglycemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy: A Consensus Statement of the American Diabetes Association and the European Association for the Study of Diabetes," *Diabetes Care* 32, no. 1 (2009).

7 Jeroen Struijs et al., "Comorbidity in Patients with Diabetes Mellitus: Impact on Medical Health Care Utilization," *BMC Health Services Research* 6, no. 1 (2006).

8 Michael Shwartz et al., "The Importance of Comorbidities in Explaining Differences in Patient Costs," *Medical Care* 34, no. 8 (1996).

9 Mary E. Charlson et al., "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients," *Journal of Clinical Epidemiology* 61, no. 12 (2008).

healthcare resources could be beneficial in that 1) early identification of these patients may bring about more timely care for them, and 2) that healthcare resources may be allocated more efficiently.

Another reason to measure comorbidities has to do with its usefulness in controlling for confounding effects, especially in retrospective and observational studies. Unlike randomized controlled trials, in which subjects are usually screened by stringent inclusion and exclusion criteria, observational studies are based on "real-world" data from patients with diverse backgrounds and with different levels of health status. However, the need still exists for researchers to ascertain the baseline health status of subjects before any meaningful analyses can be conducted. Theoretically, the confounding effects resulting from the differences in patient characteristics can be minimized thorough randomization, but this approach may not always be feasible. In retrospective studies, random allocation of patients to treatment and control groups is rarely possible. The study objective may be to examine effectiveness in a "real-world" setting but not efficacy in a controlled setting. In addition, researchers may not have the luxury of excluding patients who are too sick because the sample size might become too small or the generalizability could be compromised. Hence, an alternate approach is to include comorbidities as a covariate and other risk factors in statistical models when "real-world" data are analyzed. Once the assumption of homogeneity across groups is satisfied, researchers can be more confident in exploring the true relationships between

[10] Shwartz et al., "The Importance of Comorbidities in Explaining Differences in Patient Costs."

the independent and dependent variables and making reasonable and meaningful comparisons and inferences.

1.2.3 Comorbidity Adjustment Measures

Like other risk factors, comorbidity assessment can be useful when it is properly identified and quantified. However, measuring comorbidities could be challenging because comorbid conditions may not be determined as easily as other risk factors such as age and sex. For instance, comorbidities may not be documented completely in an emergency department setting because time is limited and the focus of care is to alleviate an immediate ailment as rapidly as possible. Acute comorbidities are less likely to be recognized than chronic comorbidities because they may have resolved before or between clinic visits. Nevertheless, given the aforementioned reasons to measure comorbidity, researchers have attempted to develop methods to quantify comorbidities systematically. These measures are commonly referred to as comorbidity index, comorbidity score, severity measure, severity score, or risk adjustment tool, among others. Given the lack of consistent terminology, the following discussion will refer to these instruments as *comorbidity adjustment measures*.

The interest in developing comorbidity adjustment measures has grown over the past few decades, as these measures can be applied in several possible scenarios: comparison of comorbidity and general health status across patient groups; matching of subjects in case-control studies; setting reimbursement rates for hospitals or clinics; and evaluation of patient characteristics of respondents and non-respondents in survey

research. Compared to subjective clinical judgment of patient health status, the use of comorbidity adjustment measures is advantageous in that the chance of bias is minimized, since the evaluation of patients' comorbidities is based on systematic reviews with predefined methodology.

Further, because most of these measures produce a single composite numerical score, statistical efficiency is enhanced when these measures are applied in studies employing statistical models. This characteristic makes comorbidity adjustment measures particularly attractive when the study sample sizes are relatively small or when multiple hypotheses need to be tested. A single summary score enables researchers to adjust for patient comorbidity with only one variable, which in turn simplifies the process of model building as the number of covariates decreases significantly. Granted, information may be lost when a single numerical score is used to reflect such a complex construct, but on the other hand, trying to code every comorbid condition as a separate variable in statistical models may result in model over-fitting. Therefore, comorbidity adjustment measures may be preferable in research utilizing large databases, where analyses can be conducted on a considerable amount of information within a relatively short time period and at a minimal cost.

One convenient way to quantify comorbidity is through a simple count of the number of comorbid conditions. However, this method fails to account for the varying degrees of severity inherent in different disease states. In order to account for the severity of diseases, Kaplan and Feinstein created one of the earliest comorbidity adjustment measures, which classifies comorbidities in diabetic patients through a scoring system

based on clinical consensual judgment.[11] Over the years, myriad similar measures have been developed to assess comorbidities in patients with different diseases and in different settings.

Generally, comorbidity adjustment measures can be categorized based on the type of data used to derive the measures and the designated purposes of the measures. Comorbidity adjustment measures are usually based on two types of data: clinical diagnoses, which can be ascertained using the International Classification of Diseases (ICD) codes, or medication utilization, which can be identified using the American Hospital Formulary Service (AHFS) classification codes. The availability of diagnosis- and medication-based measures means that researchers may opt for either type of measure depending on what type of data are available. Depending on the purpose of a measure, it can also be classified as a general-purpose or a disease-specific measure. General-purpose comorbidity adjustment measures presumably may be used for any disease state and in any patient population, even though the development of these measures is invariably based on a pilot patient population of a certain disease. In contrast, disease-specific measures are designed to be used in patients with a particular disease. Arguably, disease-specific measures could better reflect comorbidities in a subgroup of patients than general-purpose measures because the distribution of comorbidities is likely to vary across patient populations with different disease states.

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[11] Moreson H. Kaplan and Alvan R. Feinstein, "The Importance of Classifying Initial Co-Morbidity in Evaluating the Outcome of Diabetes Mellitus," *Journal of Chronic Diseases* 27 (1974).

Although many proprietary and non-proprietary comorbidity adjustment measures have been developed and made available to researchers, the following discussion will focus on two general-purpose comorbidity adjustment measures that have been used extensively. One is the Charlson Comorbidity Index (CCI), a measure that is based on clinical diagnoses; the other is the Chronic Disease Score (CDS), which produces a summary comorbidity score based on medication use from pharmacy data.

1.2.3.1 Charlson Comorbidity Index

The CCI was developed empirically by Charlson and her colleagues, who examined the medical records of a cohort of patients admitted in a New York hospital to derive a weighted comorbidity index. Charlson et al. selected comorbid conditions that were presumably predictive of one-year mortality in the test group and subsequently validated the index in another group of patients with breast cancer.[12] Based on the adjusted relative risks from the regression model, 19 comorbid conditions were assigned weights of one, two, three, or six.[13] A composite score is produced for each patient by summing up the scores corresponding to the comorbid conditions the patient has. A lower CCI score is associated with a lower mortality rate in the following year. Conversely, a higher CCI score is predictive of a higher one-year mortality rate after the index year.

Although the CCI reasonably predicts one-year mortality with a simple composite score, researchers need to review medical records and identify all relevant diagnoses of

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[12] Mary E. Charlson et al., "A New Method of Classifying Prognostic Comorbidity in Longitudinal Studies: Development and Validation," *Journal of Chronic Diseases* 40, no. 5 (1987).

[13] Ibid.

comorbidities in order to calculate the index score. However, researchers may not always have access to medical records, and reviewing medical records could also be a time-consuming and tedious process. The advent of large administrative databases provides researchers with rich data sources from diverse settings that also require appropriate comorbidity adjustment. Therefore, several adaptations of the original CCI have been developed to facilitate its application in large database research; some notable versions include the Deyo, Dartmouth-Manitoba, and D'Hoore adaptations.[14,15,16]

Deyo et al. adapted the original CCI for use with ICD-9-CM diagnosis and procedure codes in a group of Medicare patients who underwent lumbar spine surgery.[17] The Deyo adaptation used weights from the CCI to obtain two index scores for each patient, one based on the ICD-9-CM codes assigned when the patient was admitted to a hospital and one based on the codes assigned during the previous year prior to the admission. Both index scores, after division into four categories (i.e., 0, 1, 2, ≥3), were found to be significantly associated with in-hospital complications, short-term mortality, blood transfusion, discharge to nursing home, hospital length of stay, and total hospital

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[14] Richard A. Deyo, Daniel C. Cherkin, and Marcia A. Ciol, "Adapting a Clinical Comorbidity Index for Use with ICD-9-CM Administrative Databases," *Journal of Clinical Epidemiology* 45 (1992).

[15] Patrick S. Romano, Leslie L. Roos, and James G. Jollis, "Further Evidence Concerning the Use of a Clinical Comorbidity Index with ICD-9-CM Administrative Data," *Journal of Clinical Epidemiology* 46, no. 10 (1993).

[16] William D'Hoore, André Bouckaert, and Charles Tilquin, "Practical Considerations on the Use of the Charlson Comorbidity Index with Administrative Data Bases," *Journal of Clinical Epidemiology* 49, no. 12 (1996).

[17] Deyo, Cherkin, and Ciol, "Adapting a Clinical Comorbidity Index for Use with ICD-9-CM Administrative Databases."

charges.[18] Although the magnitudes of these associations were not reported, the authors observed that the associations were still significant after controlling for age, which suggested that the adapted CCI explained additional variances in these variables compared to a model merely based on age.[19]

The Dartmouth-Manitoba adaptation of the CCI was developed by Romano et al., who also tried to translate the original CCI for use with administrative databases. Compared to the Deyo adaptation, Romano et al. assigned slightly different sets of ICD-9-CM codes to the comorbid conditions listed in the CCI.[20] Two large administrative databases were utilized to test the CCI's predictive ability in mortality and complications in patients undergoing coronary artery bypass graft surgery and intervertebral disc excision. The Deyo and Dartmouth-Manitoba adaptations produced similar prevalence estimates of individual comorbidities, and the overall predictive power of the CCI was comparable; however, they found that the empirical weights derived from multivariate analyses may be significantly different from those assigned in the original CCI if the outcome of interest and study population are different.[21] For example, in the original CCI weighting system, a score of one was assigned to congestive heart failure, but Romano et

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[18] Ibid.

[19] Ibid.

[20] Romano, Roos, and Jollis, "Further Evidence Concerning the Use of a Clinical Comorbidity Index with ICD-9-CM Administrative Data."

[21] Ibid.

al. postulated that the same comorbidity should be assigned a score of three in patients who just underwent coronary artery bypass graft surgery.[22]

Ghali et al. examined how at the individual patient's level, the Deyo and Dartmouth-Manitoba coding schemes agreed or disagreed with each other in producing index scores and also attempted to derive a new set of weights based on the ICD-9-CM codes using the original CCI.[23] Patients who underwent coronary artery bypass graft surgery in two separate years were selected, and the outcome of interest was in-hospital mortality. Their findings suggested that the difference between the Deyo and Dartmouth-Manitoba adaptations was minimal, as the scores agreed perfectly with each other in nine out of ten cases; they also argued that study-specific weights should be developed and used whenever possible because of improved model discrimination power.[24] In a separate study, the Deyo and Dartmouth-Manitoba adaptations were found to agree with each other more than 80 percent of the time.[25]

D'Hoore et al. also adapted the original CCI for use with administrative databases and used the ICD-9 codes without the two-digit clinical modification codes because sometimes only the first three ICD-9 codes are used or available.[26] Namely, D'Hoore's

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[22] Ibid.

[23] William A. Ghali et al., "Searching for an Improved Clinical Comorbidity Index for Use with ICD-9-CM Administrative Data," *Journal of Clinical Epidemiology* 49, no. 3 (1996).

[24] Ibid.

[25] Martin Nuttall, Jan van der Meulen, and Mark Emberton, "Charlson Scores Based on ICD-10 Administrative Data Were Valid in Assessing Comorbidity in Patients Undergoing Urological Cancer Surgery," *Journal of Clinical Epidemiology* 59, no. 3 (2006).

[26] D'Hoore, Bouckaert, and Tilquin, "Practical Considerations on the Use of the Charlson Comorbidity Index with Administrative Data Bases."

coding scheme contained less information on diagnoses and no information on procedures. Data on 33,940 patients with ischemic heart disease were analyzed, and the adapted CCI was found to be significantly associated with inpatient one-year mortality in two consecutive years.[27] D'Hoore et al.'s findings demonstrated that the predictive ability of the CCI remains reasonable without the clinical modification codes. Nevertheless, no studies had compared all three adaptations concurrently.

The CCI has also been adapted for use with ICD-10 codes,[28] but the most notable recent update was conducted by Charlson et al., who used Deyo's coding scheme to predict healthcare costs in a primary care setting.[29] They found that the adapted index was a better predictor of annual healthcare costs than a number of variables, including age, sex, and certain medications.[30] The list of comorbidities was expanded to include depression, hypertension, use of warfarin (all with a weight of one), and skin ulcers or cellulitis (with a weight of two).[31] The adaptation explained approximately one-fifth of the variance in annual healthcare costs and successfully identified patients who incurred high costs, the majority of whom were either Medicare or Medicaid beneficiaries.[32]

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[27] Ibid.

[28] Nuttall, van der Meulen, and Emberton, "Charlson Scores Based on ICD-10 Administrative Data Were Valid in Assessing Comorbidity in Patients Undergoing Urological Cancer Surgery."

[29] Charlson et al., "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients."

[30] Ibid.

[31] Ibid.

[32] Ibid.

The list of comorbid conditions and their associated weights and ICD-9 codes as assigned and adapted in different CCI adaptations are in Appendix A. Appendix B includes the four additional comorbid conditions and their associated ICD-9 code and generic code numbers.

1.2.3.2 Chronic Disease Score

Using automated pharmacy dispensing data from the Group Health Cooperative of Puget Sound, a Washington-based health maintenance organization, Von Korff et al. developed the Chronic Disease Score (CDS) that approximates an individual's health status based on the type and number of prescription medications used by a patient.[33] Medications used to treat 17 different chronic conditions over a one-year period were identified, and weights were assigned by consensus judgment in order to calculate a total chronic disease score. The CDS was found to be a stable measure associated with patient health status and predictive of mortality and hospitalization rates after controlling for age and sex. A patient with a higher CDS has poorer health status and is more likely to die or be hospitalized. Appendix C provides a detailed list of chronic conditions, medication classes, and weights used in the CDS.

Clark et al. revised the original CDS by including more disease states (i.e., depression and other mental illnesses) and the list of medications for severity scoring; they also used empirically derived weights as opposed to the weights assigned based on

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[33] Michael Von Korff, Edward H. Wagner, and Kathleen Saunders, "A Chronic Disease Score from Automated Pharmacy Data," *Journal of Clinical Epidemiology* 45, no. 2 (1992).

clinical judgment.[34] Outpatient drug utilization data over a six-month period were examined to develop the revised CDS to predict total cost, outpatient care cost, and primary care visits.[35] Compared to the original CDS, the revised CDS explained a higher proportion of variance in all three outcome variables both concurrently and prospectively; although a different method called the ambulatory diagnostic groups (ADGs) performed better than the revised CDS in explaining concurrent outpatient cost and primary care visits, the revised CDS explained more variance in total and outpatient costs than the ADGs in the prospective model.[36] The revised CDS was also found to be associated with mortality and hospitalizations.[37] Appendix D illustrates the list of chronic conditions, medication classes, and regression weights for prediction of total cost, outpatient cost, and primary care visits in the revised CDS.

1.2.4 Assessing Comorbidity Adjustment Measures

While comorbidity adjustment measures have been increasingly used in epidemiological and outcomes research, some have argued that the utility of these measures might be limited. Schneeweiss and Maclure contended that comorbidity adjustment measures should only be used in exploratory data analyses because a single composite score, as produced by most measures, could oversimplify a complex construct

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[34] Daniel O. Clark et al., "A Chronic Disease Score with Empirically Derived Weights," *Medical Care* 33, no. 8 (1995).

[35] Ibid.

[36] Ibid.

[37] Ibid.

like comorbidity and erroneously assume that the effects of comorbidities would be constant across different patient populations.[38] Martins and Blais tested the CCI in a Brazilian population and found that different weights should be assigned to the original predictors in order to achieve optimal prediction of in-hospital mortality; they argued that some of the original predictors should be dropped and new predictors included.[39] It has been proposed that a predictive statistical model similar to the CCI cannot explain more than 20% of the variance in patient healthcare expenditures.[40]

One major limitation of these measures is that their predictive performance is only as good as the data quality. Ideally, administrative databases should contain all relevant information on patient encounters, including demographic characteristics, health status, prior medical history, and medication use. However, rarely do researchers come across such a comprehensive database because the purpose of these databases is primarily for claims processing, and recording an excess amount of information is unnecessary and impractical. Coding errors are common, and under-coding of diagnoses is possible. One study compared the CCI derived from medical records with that from administrative databases and found that medical record data produced a CCI score that was more

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[38] Sebastian Schneeweiss and Malcolm Maclure, "Use of Comorbidity Scores for Control of Confounding in Studies Using Administrative Databases," *International Journal of Epidemiology* 29 (2000).

[39] Mônica Martins and Régis Blais, "Evaluation of Comorbidity Indices for Inpatient Mortality Prediction Models," *Journal of Clinical Epidemiology* 59, no. 7 (2006).

[40] Rene C. J. A. van Vliet, "Predictability of Individual Helath Care Expenditures," *The Journal of Risk and Insurance* 59, no. 3 (1992).

powerful in predicting mortality and hospital length of stay, possibly because less information is recorded in the claims file of administrative databases.[41]

Comorbidity adjustment measures have other limitations. First, their predictive power is sensitive to changes in study time frame: while the CCI is a reasonable predictor of one-year mortality, the Deyo and Dartmouth-Manitoba CCI adaptations predict 30-day, 90-day, and 180-day mortalities poorly.[42] Second, classification of comorbidity based on pharmacy data could be problematic because medication-based measures generally do not include non-prescription drugs, and some medications may have multiple indications or off-label uses. Third, any given comorbidity adjustment measure could only contain a limited list of comorbid conditions, and the range of these conditions could be more applicable in one patient population than another due to their associations with the principal diagnosis under investigation. The inclusion of additional comorbid conditions could improve a measure's predictive power, albeit with ceiling effects.[43]

As such, it is desirable to examine the utilities of comorbidity adjustment measures, especially when they are to be used to predict a different outcome, in a different population, or with a different time frame. Indeed, an increasing body of literature has been dedicated to the evaluation of available measures.[44,45] Of particular

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41 Stephanie M. Kieszak et al., "A Comparison of the Charlson Comorbidity Index Derived from Medical Record Data and Administrative Billing Data," *Journal of Clinical Epidemiology* 52, no. 2 (1999).

42 Mario A. Cleves, Nena Sanchez, and Mayumi Draheim, "Evaluation of Two Competing Methods for Calculating Charlson's Comorbidity Index When Analyzing Short-Term Mortality Using Administrative Data," *Journal of Clinical Epidemiology* 50, no. 8 (1997).

43 Martins and Blais, "Evaluation of Comorbidity Indices for Inpatient Mortality Prediction Models."

44 Ronald Gijsen et al., "Causes and Consequences of Comorbidity: A Review," *Journal of Clinical Epidemiology* 54, no. 7 (2001).

interest, though, are empirical validation studies that compare two or more measures side by side in order to establish their relative performance. Such studies could provide valuable findings to researchers who need to choose a comorbidity adjustment measure that would align appropriately with their study objectives. Some studies have compared different types of diagnosis-based measures,[46,47] while others compared diagnosis-based measures with medication-based measures.[48,49] Despite the popularity of the CCI and CDS, only a few researchers have compared these two measures with each other.[50,51] Further, no evaluations have been made on these two measures' predictive ability in patients with diabetes, even though diabetes is a prevalent chronic disease that has been studied extensively in outcomes and epidemiological research.[52,53]

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45 Vincent de Groot et al., "How to Measure Comorbidity: A Critical Review of Available Methods," *Journal of Clinical Epidemiology* 56 (2003).

46 Yan Yan et al., "Comorbidity Indices to Predict Mortality from Medicare Data," *Medical Care* 43, no. 11 (2005).

47 Jun Tang, Jim Y. Wan, and James E. Bailey, "Performance of Comorbidity Measures to Predict Stroke and Death in a Community-Dwelling, Hypertensive Medicaid Population," *Stroke* 39 (2008).

48 Terry L. Wahls, Mitchell J. Barnett, and Gary E. Rosenthal, "Predicting Resource Utilization in a Veterans Health Administration Primary Care Population: Comparison of Methods Based on Diagnoses and Medications," *Medical Care* 42, no. 2 (2004).

49 Joel F. Farley, Carolyn R. Harley, and Joshua W. Devine, "A Comparison of Comorbidity Measurements to Predict Healthcare Expenditures," *American Journal of Managed Care* 12, no. 2 (2006).

50 Anthony J. Perkins et al., "Common Comorbidity Scores Were Similar in Their Ability to Predict Health Care Costs and Mortality," *Journal of Clinical Epidemiology* 57 (2004).

51 Sebastian Schneeweiss et al., "Performance of Comorbidity Scores to Control for Confounding in Epidemiologic Studies Using Claims Data," *American Journal of Epidemiology* 154, no. 9 (2001).

52 Julie S. Krop et al., "Patterns of Expenditures and Use of Services among Older Adults with Diabetes. Implications for the Transition to Capitated Managed Care," *Diabetes Care* 21, no. 5 (2005).

53 Rajesh Balkrishnan et al., "Predictors of Medication Adherence and Associated Health Care Costs in an Older Population with Type 2 Diabetes Mellitus: A Longitudinal Cohort Study," *Clinical Therapeutics* 25, no. 11 (2003).

1.3 DIABETES

1.3.1 Definition and Diagnostic Criteria for Diabetes

Diabetes mellitus is a metabolic illness characterized by abnormally high blood glucose levels. Although some patients cannot be categorized easily into a specific type of diabetes, diabetes can be broadly classified into four clinical classifications based on its etiology: type 1 diabetes, caused by insufficient insulin production due to the loss of pancreatic beta cells; type 2 diabetes, caused by increased resistance or reduced sensitivity to insulin; gestational diabetes, any degree of glucose intolerance diagnosed during pregnancy; and other types of diabetes, induced by drugs or other disease states that impair pancreatic function.[54]

A diagnosis of diabetes is made if a patient meets one of the diagnostic criteria in repeated tests: fasting plasma glucose level is equal to or higher than 126 mg/dl (7.0 mmol/l); symptoms of hyperglycemia are presented with a random plasma glucose level equal to or higher than 200 mg/dl (11.1 mmol/l); or the two-hour plasma glucose level is equal to or higher than 200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test.[55] Patients are diagnosed as pre-diabetic if their fasting plasma glucose levels fall between 100 mg/dl (5.6 mmol/l) and 125 mg/dl (6.9 mmol/l) or if the two-hour plasma glucose

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[54] Nathan et al., "Medical Management of Hyperglycemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy: A Consensus Statement of the American Diabetes Association and the European Association for the Study of Diabetes."

[55] Ibid.

levels are between 140 mg/dl (7.8 mmol/l) and 199 mg/dl (11.0 mmol/l); pre-diabetes is associated with increased risks for diabetes and cardiovascular disease.[56]

1.3.2 Treatment for Diabetes

The choice of treatment for diabetes is principally dependent upon the type of diabetes presented by the patient, but other clinical (e.g., side effects of medications) and non-clinical factors (e.g., cost of treatment) are also taken into consideration in the decision process. Nevertheless, the overarching goals in treating different types of diabetes are to achieve and maintain appropriate blood glucose and hemoglobin A1C levels.

The treatment for patients with type 1 diabetes includes insulin through injections or continuous subcutaneous infusion pumps, matching of after-meal insulin to food and physical activity, and insulin analogues.[57] The management of type 2 diabetes employs a step-wise approach: the first line of therapy is a combination of lifestyle interventions and metformin. Insulin, sulfonylureas, pioglitazone, or exenatide may be employed as an additional therapy if glycemic goals are not achieved; a triple pharmacologic therapy consisting of metformin, pioglitazone, and a sulfonylurea may be considered but is not recommended; and all patients should be placed on metformin and intensive insulin

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[56] Ibid.

[57] Ibid.

therapy if poor glycemic control persists.[58] The treatment for gestational diabetes includes lifestyle interventions and/or insulin injections.[59]

1.3.3 Epidemiology and Economic Burden of Diabetes

From 1980 to 2006, the number of Americans who were diagnosed with diabetes increased three-fold, and the prevalence rate more than doubled.[60] While improvements in diagnostic techniques and longer life expectancy may be attributed to the increased prevalence of diabetes, the rising number of diabetic individuals in the United States may also be a result of sedentary lifestyles and widespread obesity. In 2007, an estimated 17.5 million people, or 5.8 percent of the U.S. population, had been diagnosed with diabetes, reflecting a growth rate of approximately one million new cases per year since 2002; if those who were afflicted by the disease but undiagnosed were taken into account, then the total prevalence rate would increase to 8 percent.[61] A recent estimate predicted that 48.3 million people, or 12 percent of the U.S. population, will be diagnosed with diabetes by 2050.[62] People who are older or of African American origin are more likely to suffer

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[58] Ibid.

[59] Ibid.

[60] Centers for Disease Control and Prevention. "Number (in Millions) of Civilian/Noninstitutionalized Persons with Diagnosed Diabetes, United States, 1980–2006." http://www.cdc.gov/diabetes/statistics/prev/national/figpersons.htm (accessed March 1, 2009).

[61] American Diabetes Association, "Economic Costs of Diabetes in the U.S. In 2007," *Diabetes Care* 31, no. 3 (2008).

[62] K. M. Venkat Narayan et al., "Impact of Recent Increase in Incidence on Future Diabetes Burden," *Diabetes Care* 29, no. 9 (2006).

from diabetes;[63,64] males are slightly more likely than females to develop diabetes.[65] Diabetes is the sixth leading cause of death in the U.S.[66]

Diabetes is a costly illness that burdens both patients and their families medically and economically. In 2007, the national total cost of diabetes was estimated to be $174 billion, where $116 billion was attributed to direct medical costs and $58 billion was indirect costs related to reduced productivity, work loss, and premature mortality.[67] For every 10 dollars spent on health care in the U.S., two dollars were spent by people with diabetes, of which one dollar was directly attributable to diabetes mainly because of the increased hospital admission rate and longer hospital length of stay.[68] More significantly, diabetic patients incurred healthcare expenditures that were 2.3 times higher than those without diabetes.[69]

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63 Centers for Disease Control and Prevention. "Percentage of Civilian, Noninstitutionalized Population with Diagnosed Diabetes, by Age, United States, 1980–2006." http://www.cdc.gov/diabetes/statistics/prev/national/figbyage.htm (accessed March 1, 2009).

64 Centers for Disease Control and Prevention. "Age-Adjusted Percentage of Civilian, Noninstitutionalized Population with Diagnosed Diabetes, by Race and Sex, United States, 1980–2006." http://www.cdc.gov/diabetes/statistics/prev/national/figraceethsex.htm (accessed March 1, 2009).

65 Centers for Disease Control and Prevention. "Age-Adjusted Percentage of Civilian, Noninstitutionalized Population with Diagnosed Diabetes, by Sex, United States, 1980–2006." http://www.cdc.gov/diabetes/statistics/prev/national/figbysex.htm (accessed March 1, 2009).

66 Hsiang-Ching Kung et al., "National Vital Statistics Reports - Deaths: Final Data for 2005," ed. Centers for Disease Control and Prevention (2008).

67 American Diabetes Association, "Economic Costs of Diabetes in the U.S. In 2007."

68 Ibid.

69 Ibid.

1.3.4 Reasons to Measure Comorbidity in Persons with Diabetes

Measuring comorbidities in diabetic patients is important for several reasons. First, diabetic patients often endure multiple comorbid conditions, and research on diabetes requires the careful consideration of comorbidities and their effects on patients. Ninety-six percent of Medicare beneficiaries with type 2 diabetes have at least one comorbidity, 46 percent suffer from five or more comorbidities, and about one in ten have more than ten comorbid conditions.[70] In a Dutch population, almost half of the patients with diabetes had at least one comorbid condition.[71] Further, diabetic patients are more likely to have depression,[72] hypertension,[73] coronary heart disease,[74] and hip fractures[75] than non-diabetic patients. Thus, research on diabetes is likely to be influenced by the confounding and mediating effects from comorbidities, and failure to control for such effects may bias study findings and interpretations. Although the importance of

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[70] Marlene R. Niefeld et al., "Preventable Hospitalization among Elderly Medicare Beneficiaries with Type 2 Diabetes," *Diabetes Care* 26, no. 5 (2003).

[71] Struijs et al., "Comorbidity in Patients with Diabetes Mellitus: Impact on Medical Health Care Utilization."

[72] Leonard E. Egede, Deyi Zheng, and Kit Simpson, "Comorbid Depression Is Associated with Increased Health Care Use and Expenditures in Individuals with Diabetes," *Diabetes Care* 25, no. 3 (2002).

[73] David M. Maahs et al., "Hypertension Prevalence, Awareness, Treatment, and Control in an Adult Type 1 Diabetes Population and a Comparable General Population," *Diabetes Care* 28, no. 2 (2005).

[74] Frank B. Hu et al., "The Impact of Diabetes Mellitus on Mortality from All Causes and Coronary Heart Disease in Women: 20 Years of Follow-Up," *Archives of Internal Medicine* 161, no. 14 (2001).

[75] Lorraine L. Lipscombe et al., "The Risk of Hip Fractures in Older Individuals with Diabetes: A Population-Based Study," *Diabetes Care* 30, no. 4 (2007).

accounting for comorbidity in the treatment of diabetes has long been recognized, its role in statistical analyses received attention much later.[76]

Moreover, the coexistence of diabetes and comorbidities not only complicates the management of diabetes itself but also the treatment of the comorbid conditions. Patients who suffer from diabetes and other chronic diseases are less likely to receive treatments for other unrelated comorbid conditions.[77] Under-diagnosis of comorbidities is common: about 45 percent of adult patients with both depression and diabetes have their depression undiagnosed and thus untreated.[78] Even if depression is diagnosed, diabetic patients who have comorbid depression still have poorer quality of life[79] and worse adherence to antidiabetic medications[80] or glucose self-monitoring regimens.[81] As such, timely identification and effective management of comorbidities in persons with diabetes seem to be a potential area of care where patient outcomes could be greatly improved.

Studying diabetes and its comorbidities also has important implications in health services research. As mentioned earlier, diabetes is a costly disease, yet diabetic patients

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[76] Kaplan and Feinstein, "The Importance of Classifying Initial Co-Morbidity in Evaluating the Outcome of Diabetes Mellitus."

[77] Donald A. Redelmeier, Siew H. Tan, and Gillian L. Booth, "The Treatment of Unrelated Disorders in Patients with Chronic Medical Diseases," *New England Journal Medicine* 338, no. 21 (1998).

[78] Chaoyang Li et al., "Prevalence and Correlates of Undiagnosed Depression among U.S. Adults with Diabetes: The Behavioral Risk Factor Surveillance System, 2006," *Diabetes Research and Clinical Practice* 83, no. 2 (2009).

[79] Robert D. Goldney et al., "Diabetes, Depression, and Quality of Life: A Population Study," *Diabetes Care* 27, no. 5 (2004).

[80] Elizabeth H. B. Lin et al., "Relationship of Depression and Diabetes Self-Care, Medication Adherence, and Preventive Care," *Diabetes Care* 27, no. 9 (2004).

[81] Jeffrey S. Gonzalez et al., "Depression, Self-Care, and Medication Adherence in Type 2 Diabetes: Relationships across the Full Range of Symptom Severity," *Diabetes Care* 30, no. 9 (2007).

seem to differ in their utilization of healthcare services depending on whether or not they have comorbidities. For example, diabetic patients with depression visit ambulatory care more often and have more prescriptions than those without depression; total health expenditures for patients with depression are 4.5 times higher compared to those without depression.[82] In addition, as the severity of depression increases, the total of incurred healthcare costs also increase.[83] Cardiovascular-related comorbidities, such as congestive heart failure and hypertension, are associated with increased odds of hospitalizations that may be prevented.[84] Diabetic patients with non-cardiovascular type of comorbidities, such as musculoskeletal diseases and cancer, were found to have more hospital admissions and a longer hospital length of stay.[85] One study using data from Medicare patients showed that about 7% of hospitalizations could be avoided in patients with type 2 diabetes if both cardiovascular and non-cardiovascular related comorbidities were addressed clinically.[86]

In summary, because comorbidities are prevalent among diabetic patients, it is important to understand diabetes care within the context of comorbidities, and studies on diabetes and its comorbidities could bring potential benefits to various stakeholders:

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[82] Egede, Zheng, and Simpson, "Comorbid Depression Is Associated with Increased Health Care Use and Expenditures in Individuals with Diabetes."

[83] Paul S. Ciechanowski, Wayne J. Katon, and Joan E. Russo, "Depression and Diabetes: Impact of Depressive Symptoms on Adherence, Function, and Costs," *Archives of Internal Medicine* 160, no. 21 (2000).

[84] Niefeld et al., "Preventable Hospitalization among Elderly Medicare Beneficiaries with Type 2 Diabetes."

[85] Struijs et al., "Comorbidity in Patients with Diabetes Mellitus: Impact on Medical Health Care Utilization."

[86] Niefeld et al., "Preventable Hospitalization among Elderly Medicare Beneficiaries with Type 2 Diabetes."

clinicians could devise better treatment and management plans for diabetic patients with comorbid conditions; researchers could improve statistical analyses and data interpretation by appropriately adjusting for comorbidities; and policy makers could identify and address areas of diabetes care to promote more efficient use of health services. To enhance the understanding of comorbidities and their effects on healthcare utilization in diabetic patients, a large health insurer such as the Department of Defense TRICARE program would provide a rich data source for comparisons of different comorbidity adjustment measures.

1.4 DEPARTMENT OF DEFENSE TRICARE PROGRAM

The TRICARE program is an integrated healthcare program within the Military Health System of the United States Department of Defense (DoD). It is managed by the TRICARE Management Activity under the Assistant Secretary of Defense for Health Affairs of the DoD and funded in large part by the Defense Health Program Operations and Maintenance appropriation.[87] Historically, healthcare benefits for military retirees and family members were provided by the Civilian Health and Medical Program of the Uniformed Services (CHAMPUS), created through the passages of the Dependents Medical Care Act in 1956 and the Military Medical Benefits Amendments in 1966.[88] In order to improve access to care and minimize costs, TRICARE was created in 1994 to replace CHAMPUS.[89] It is a large network of healthcare resources drawn from the military forces and civilian health plans, providing comprehensive healthcare benefits to approximately 9.4 million beneficiaries worldwide, including active military personnel and their dependents, retirees and their dependents, and survivors.[90]

Beneficiaries who are not Medicare-eligible may choose from one of the three TRICARE options, each with its own fee structure: TRICARE Prime, a health maintenance organization-type option; TRICARE Extra, a preferred provider option; and

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87 Department of Defense TRICARE. "What is TRICARE?" http://tricare.mil/mybenefit/home/overview/WhatIsTRICARE? (accessed March 30, 2009).

88 Ibid.

89 Ibid.

90 Ibid.

TRICARE Standard, a fee-for-service option.[91] In 2001, TRICARE for Life was initiated as a secondary payer to cover out-of-pocket expenses for those who are dually eligible for Medicare and TRICARE.[92] In the United States, TRICARE is managed in three separate regions by three managed care contractors: Health Net (north), Humana (south), and TriWest (west).[93] In fiscal year 2005, approximately 40 percent of the TRICARE beneficiaries were active duty personnel and dependents, while the other 60 percent were retirees and their dependents or TRICARE for Life retirees and dependents.[94]

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[91] Department of Defense TRICARE. "TRICARE Plans." http://tricare.mil/mybenefit/home/overview/Plans (accessed March 30, 2009).

[92] Department of Defense TRICARE. "TRICARE for Life." http://tricare.mil/mybenefit/home/overview/Plans/ForLife? (accessed March 30, 2009).

[93] Department of Defense TRICARE. "TRICARE Regions." http://tricare.mil/mybenefit/home/overview/Regions? (accessed March 30, 2009).

[94] United States Government Accountability Office, "Defense Health Care: Access to Care for Beneficiaries Who Have Not Enrolled in Tricare's Managed Care Option," (2006).

1.5 STUDY RATIONALE

As mentioned earlier, no studies have compared the utility of the Charlson Comorbidity Index and the Chronic Disease Score in predicting health-related outcomes for diabetic patients. One recent study found that the Charlson Comorbidity Index had similar utility in the prediction of healthcare expenditures among diabetic patients when compared with RxRisk-V, a medication-based adjustment measure.[95] However, this study did not test the updated version of the Charlson Comorbidity Index nor include the Chronic Disease Score. In addition, the study was based on a Veteran population that was predominantly male.

The current study compared the Charlson Comorbidity Index with the Chronic Disease Score using a nationally representative sample of TRICARE patients with diabetes. The study findings could help validate the updated version of the Charlson Comorbidity Index and also provide empirical evidence for choosing an appropriate comorbidity adjustment measure in health services and epidemiological research involving diabetic patients.

[95] Matthew L. Maciejewski, Chuan-Fen Liu, and Stephan D. Fihn, "Performance of Comorbidity, Risk Adjustment, and Functional Status Measures in Expenditure Prediction for Patients with Diabetes," *Diabetes Care* 32, no. 1 (2009).

1.6 OBJECTIVES

The purpose of this study was to analyze the utility of the number of distinct medications, index-year total healthcare expenditures, Charlson Comorbidity Index (CCI), and the Chronic Disease Score (CDS) in predicting healthcare utilization and expenditures in patients with diabetes. Two adaptations of the CCI were used: the Deyo adaption and Charlson et al.'s 2008 adaptation, referred to as CCI-1 and CCI-2 respectively hereafter. Both versions of the CDS were used, referred to as CDS-1 and CDS-2 hereafter. Data from the DoD TRICARE program were used to examine the measures' predictive performance in one-year and two-year 1) total healthcare expenditures and high-expenditure individuals, 2) number and risk of hospitalizations, and 3) number and risk of emergency department visits.

Three specific study objectives were to:

1) Validate the CCI-2's use in predicting one-year and two-year healthcare utilization and expenditures;

2) Compare the use of six methods – index-year number of distinct medications, index-year total healthcare expenditures, CCI-1, CCI-2, CDS-1, and CDS-2 – in predicting future healthcare utilization and expenditures, after controlling for age and sex; and

3) Evaluate whether combining a diagnosis-based measure (i.e., CCI) with a medication-based measure (i.e., CDS) produces significantly better predictive powers than using only a diagnosis-based or medication-based measure.

1.7 HYPOTHESES

One-Year Total Healthcare Expenditures

H_1: Age and sex together significantly predict one-year total healthcare expenditures.

$Model_1$: One-year total healthcare expenditures = age + sex

H_2: The number of distinct medications in the index period is a significant predictor of one-year total healthcare expenditures, controlling for age and sex.

$Model_2$: One-year total healthcare expenditures = age + sex + number of distinct medications

H_3: The sum of total healthcare expenditures in the index period is a significant predictor of one-year total healthcare expenditures, controlling for age and sex.

$Model_3$: One-year total healthcare expenditures = age + sex + index-year total healthcare expenditures

H_4: CCI-1 is a significant predictor of one-year total healthcare expenditures, controlling for age and sex.

$Model_4$: One-year total healthcare expenditures = age + sex + CCI-1

H_5: CCI-2 is a significant predictor of one-year total healthcare expenditures, controlling for age and sex.

$Model_5$: One-year total healthcare expenditures = age + sex + CCI-2

H_6: CDS-1 is a significant predictor of one-year total healthcare expenditures, controlling for age and sex.

$Model_6$: One-year total healthcare expenditures = age + sex + CDS-1

H_7: CDS-2 is a significant predictor of one-year total healthcare expenditures, controlling for age and sex.

$Model_7$: One-year total healthcare expenditures = age + sex + CDS-2

H_8: Age, sex, the number of distinct medications, and index-year total healthcare expenditures together significantly predict one-year total healthcare expenditures.

$Model_8$: One-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures

H_9: CCI-1 is a significant predictor of one-year total healthcare expenditures, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_9$: One-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1

H_{10}: CCI-2 is a significant predictor of one-year total healthcare expenditures, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{10}$: One-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2

H_{11}: CDS-1 is a significant predictor of one-year total healthcare expenditures, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{11}$: One-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-1

H_{12}: CDS-2 is a significant predictor of one-year total healthcare expenditures, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{12}$: One-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-2

H_{13}: CDS-1 is a significant predictor of one-year total healthcare expenditures, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{13}$: One-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-1

H_{14}: CDS-2 is a significant predictor of one-year total healthcare expenditures, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{14}$: One-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-2

H_{15}: CDS-1 is a significant predictor of one-year total healthcare expenditures, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{15}$: One-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-1

H_{16}: CDS-2 is a significant predictor of one-year total healthcare expenditures, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{16}$: One-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-2

One-Year High Healthcare Expenditures: greater than or equal to the 90th percentile of one-year total healthcare expenditures

H_{17}: Age and sex together significantly predict one-year high healthcare expenditures.

$Model_{17}$: One-year high total healthcare expenditures = age + sex

H_{18}: The number of distinct medications in the index period is a significant predictor of one-year high healthcare expenditures, controlling for age and sex.

$Model_{18}$: One-year high healthcare expenditures = age + sex + number of distinct medications

H_{19}: The sum of total healthcare expenditures in the index period is a significant predictor of one-year high healthcare expenditures, controlling for age and sex.

$Model_{19}$: One-year high healthcare expenditures = age + sex + index-year total healthcare expenditures

H_{20}: CCI-1 is a significant predictor of one-year high healthcare expenditures, controlling for age and sex.

$Model_{20}$: One-year high healthcare expenditures = age + sex + CCI-1

H_{21}: CCI-2 is a significant predictor of one-year high healthcare expenditures, controlling for age and sex.

$Model_{21}$: One-year total high healthcare expenditures = age + sex + CCI-2

H_{22}: CDS-1 is a significant predictor of one-year high healthcare expenditures, controlling for age and sex.

$Model_{22}$: One-year high healthcare expenditures = age + sex + CDS-1

H_{23}: CDS-2 is a significant predictor of one-year high healthcare expenditures, controlling for age and sex.

$Model_{23}$: One-year high healthcare expenditures = age + sex + CDS-2

H_{24}: Age, sex, the number of distinct medications, and index-year total healthcare expenditures together significantly predict one-year high total healthcare expenditures.

$Model_{24}$: One-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures

H_{25}: CCI-1 is a significant predictor of one-year high healthcare expenditures, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{25}$: One-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1

H_{26}: CCI-2 is a significant predictor of one-year high healthcare expenditures, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{26}$: One-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2

H_{27}: CDS-1 is a significant predictor of one-year high healthcare expenditures, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{27}$: One-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-1

H_{28}: CDS-2 is a significant predictor of one-year high healthcare expenditures, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{28}$: One-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-2

H_{29}: CDS-1 is a significant predictor of one-year high healthcare expenditures, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{29}$: One-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-1

H_{30}: CDS-2 is a significant predictor of one-year high healthcare expenditures, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{30}$: One-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-2

H_{31}: CDS-1 is a significant predictor of one-year high healthcare expenditures, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{31}$: One-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-1

H_{32}: CDS-2 is a significant predictor of one-year high healthcare expenditures, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{32}$: One-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-2

Two-Year Total Healthcare Expenditures

H_{33}: Age and sex together significantly predict two-year total healthcare expenditures.

$Model_{33}$: Two-year total healthcare expenditures = age + sex

H_{34}: The number of distinct medications in the index period is a significant predictor of two-year total healthcare expenditures, controlling for age and sex.

$Model_{34}$: Two-year total healthcare expenditures = age + sex + number of distinct medications

H_{35}: The sum of total healthcare expenditures in the index period is a significant predictor of two-year total healthcare expenditures, controlling for age and sex.

$Model_{35}$: Two-year total healthcare expenditures = age + sex + index-year total healthcare expenditures

H_{36}: CCI-1 is a significant predictor of two-year total healthcare expenditures, controlling for age and sex.

$Model_{36}$: Two-year total healthcare expenditures = age + sex + CCI-1

H_{37}: CCI-2 is a significant predictor of two-year total healthcare expenditures, controlling for age and sex.

$Model_{37}$: Two-year total healthcare expenditures = age + sex + CCI-2

H_{38}: CDS-1 is a significant predictor of two-year total healthcare expenditures, controlling for age and sex.

$Model_{38}$: Two-year total healthcare expenditures = age + sex + CDS-1

H_{39}: CDS-2 is a significant predictor of two-year total healthcare expenditures, controlling for age and sex.

$Model_{39}$: Two-year total healthcare expenditures = age + sex + CDS-2

H_{40}: Age, sex, the number of distinct medications, and index-year total healthcare expenditures together significantly predict two-year total healthcare expenditures.

$Model_{40}$: Two-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures

H_{41}: CCI-1 is a significant predictor of two-year total healthcare expenditures, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{41}$: Two-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1

H_{42}: CCI-2 is a significant predictor of two-year total healthcare expenditures, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{42}$: Two-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2

H_{43}: CDS-1 is a significant predictor of two-year total healthcare expenditures, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{43}$: Two-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-1

H_{44}: CDS-2 is a significant predictor of two-year total healthcare expenditures, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{44}$: Two-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-2

H_{45}: CDS-1 is a significant predictor of two-year total healthcare expenditures, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{45}$: Two-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-1

H_{46}: CDS-2 is a significant predictor of two-year total healthcare expenditures, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{46}$: Two-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-2

H_{47}: CDS-1 is a significant predictor of two-year total healthcare expenditures, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{47}$: Two-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-1

H_{48}: CDS-2 is a significant predictor of two-year total healthcare expenditures, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{48}$: Two-year total healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-2

Two-Year High Healthcare Expenditures: greater than or equal to the 90th percentile of two-year total healthcare expenditures

H_{49}: Age and sex together significantly predict two-year high healthcare expenditures.

$Model_{49}$: Two-year high total healthcare expenditures = age + sex

H_{50}: The number of distinct medications in the index period is a significant predictor of two-year high healthcare expenditures, controlling for age and sex.

$Model_{50}$: Two-year high healthcare expenditures = age + sex + number of distinct medications

H_{51}: The sum of total healthcare expenditures in the index period is a significant predictor of two-year high healthcare expenditures, controlling for age and sex.

$Model_{51}$: Two-year high healthcare expenditures = age + sex + index-year total healthcare expenditures

H_{52}: CCI-1 is a significant predictor of two-year high healthcare expenditures, controlling for age and sex.

$Model_{52}$: Two-year high healthcare expenditures = age + sex + CCI-1

H_{53}: CCI-2 is a significant predictor of two-year high healthcare expenditures, controlling for age and sex.

$Model_{53}$: Two-year total high healthcare expenditures = age + sex + CCI-2

H_{54}: CDS-1 is a significant predictor of two-year high healthcare expenditures, controlling for age and sex.

$Model_{54}$: Two-year high healthcare expenditures = age + sex + CDS-1

H_{55}: CDS-2 is a significant predictor of two-year high healthcare expenditures, controlling for age and sex.

$Model_{55}$: Two-year high healthcare expenditures = age + sex + CDS-2

H_{56}: Age, sex, the number of distinct medications, and index-year total healthcare expenditures together significantly predict two-year high healthcare expenditures.

$Model_{56}$: Two-year total healthcare expenditures = age + sex + number of distinct medications + index-year high healthcare expenditures

H_{57}: CCI-1 is a significant predictor of two-year high healthcare expenditures, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{57}$: Two-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1

H_{58}: CCI-2 is a significant predictor of two-year high healthcare expenditures, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{58}$: Two-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2

H_{59}: CDS-1 is a significant predictor of two-year high healthcare expenditures, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{59}$: Two-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-1

H_{60}: CDS-2 is a significant predictor of two-year high healthcare expenditures, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{60}$: Two-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-2

H_{61}: CDS-1 is a significant predictor of two-year high healthcare expenditures, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{61}$: Two-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-1

H_{62}: CDS-2 is a significant predictor of two-year high healthcare expenditures, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{62}$: Two-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-2

H_{63}: CDS-1 is a significant predictor of two-year high healthcare expenditures, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{63}$: Two-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-1

H_{64}: CDS-2 is a significant predictor of two-year high healthcare expenditures, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{64}$: Two-year high healthcare expenditures = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-2

One-Year Number of Hospitalizations

H_{65}: Age and sex together significantly predict one-year number of hospitalizations.

$Model_{65}$: One-year number of hospitalizations = age + sex

H_{66}: The number of distinct medications in the index period is a significant predictor of one-year number of hospitalizations, controlling for age and sex.

$Model_{66}$: One-year number of hospitalizations = age + sex + number of distinct medications

H_{67}: The sum of total healthcare expenditures in the index period is a significant predictor of one-year number of hospitalizations, controlling for age and sex.

$Model_{67}$: One-year number of hospitalizations = age + sex + index-year total healthcare expenditures

H_{68}: CCI-1 is a significant predictor of one-year number of hospitalizations, controlling for age and sex.

$Model_{68}$: One-year number of hospitalizations = age + sex + CCI-1

H_{69}: CCI-2 is a significant predictor of one-year number of hospitalizations, controlling for age and sex.

$Model_{69}$: One-year number of hospitalizations = age + sex + CCI-2

H_{70}: CDS-1 is a significant predictor of one-year number of hospitalizations, controlling for age and sex.

$Model_{70}$: One-year number of hospitalizations = age + sex + CDS-1

H_{71}: CDS-2 is a significant predictor of one-year number of hospitalizations, controlling for age and sex.

$Model_{71}$: One-year number of hospitalizations = age + sex + CDS-2

H_{72}: Age, sex, the number of distinct medications, and index-year total healthcare expenditures together significantly predict one-year number of hospitalizations.

$Model_{72}$: One-year number of hospitalizations = age + sex + number of distinct medications + index-year number of hospitalizations

H_{73}: CCI-1 is a significant predictor of one-year number of hospitalizations, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{73}$: One-year number of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1

H_{74}: CCI-2 is a significant predictor of one-year number of hospitalizations, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{74}$: One-year number of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2

H_{75}: CDS-1 is a significant predictor of one-year number of hospitalizations, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{75}$: One-year number of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-1

H_{76}: CDS-2 is a significant predictor of one-year number of hospitalizations, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{76}$: One-year number of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-2

H_{77}: CDS-1 is a significant predictor of one-year number of hospitalizations, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{77}$: One-year number of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-1

H_{78}: CDS-2 is a significant predictor of one-year number of hospitalizations, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{78}$: One-year number of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-2

H_{79}: CDS-1 is a significant predictor of one-year number of hospitalizations, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{79}$: One-year number of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-1

H_{80}: CDS-2 is a significant predictor of one-year number of hospitalizations, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{80}$: One-year number of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-2

One-Year Risk of Hospitalizations: Greater than or equal to one hospital admission in one year after the index period

H_{81}: Age and sex together significantly predict one-year risk of hospitalizations.

$Model_{81}$: One-year risk of hospitalizations = age + sex

H_{82}: The number of distinct medications in the index period is a significant predictor of one-year risk of hospitalizations, controlling for age and sex.

$Model_{82}$: One-year risk of hospitalizations = age + sex + number of distinct medications

H_{83}: The sum of total healthcare expenditures in the index period is a significant predictor of one-year risk of hospitalizations, controlling for age and sex.

$Model_{83}$: One-year risk of hospitalizations = age + sex + index-year total healthcare expenditures

H_{84}: CCI-1 is a significant predictor of one-year risk of hospitalizations, controlling for age and sex.

$Model_{84}$: One-year risk of hospitalizations = age + sex + CCI-1

H_{85}: CCI-2 is a significant predictor of one-year risk of hospitalizations, controlling for age and sex.

$Model_{85}$: One-year total risk of hospitalizations = age + sex + CCI-2

H_{86}: CDS-1 is a significant predictor of one-year risk of hospitalizations, controlling for age and sex.

$Model_{86}$: One-year risk of hospitalizations = age + sex + CDS-1

H_{87}: CDS-2 is a significant predictor of one-year risk of hospitalizations, controlling for age and sex.

$Model_{87}$: One-year risk of hospitalizations = age + sex + CDS-2

H_{88}: Age, sex, the number of distinct medications, and index-year total healthcare expenditures together significantly predict one-year risk of hospitalizations.

$Model_{88}$: One-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures

H_{89}: CCI-1 is a significant predictor of one-year risk of hospitalizations, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{89}$: One-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1

H_{90}: CCI-2 is a significant predictor of one-year risk of hospitalizations, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{90}$: One-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2

H_{91}: CDS-1 is a significant predictor of one-year risk of hospitalizations, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{91}$: One-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-1

H_{92}: CDS-2 is a significant predictor of one-year risk of hospitalizations, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{92}$: One-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-2

H_{93}: CDS-1 is a significant predictor of one-year risk of hospitalizations, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{93}$: One-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-1

H_{94}: CDS-2 is a significant predictor of one-year risk of hospitalizations, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{94}$: One-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-2

H_{95}: CDS-1 is a significant predictor of one-year risk of hospitalizations, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{95}$: One-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-1

H_{96}: CDS-2 is a significant predictor of one-year risk of hospitalizations, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{96}$: One-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-2

Two-Year Number of Hospitalizations

H_{97}: Age and sex together significantly predict two-year number of hospitalizations.

$Model_{97}$: Two-year number of hospitalizations = age + sex

H_{98}: The number of distinct medications in the index period is a significant predictor of two-year number of hospitalizations, controlling for age and sex.

$Model_{98}$: Two-year number of hospitalizations = age + sex + number of distinct medications

H_{99}: The sum of total healthcare expenditures in the index period is a significant predictor of two-year number of hospitalizations, controlling for age and sex.

$Model_{99}$: Two-year number of hospitalizations = age + sex + index-year total healthcare expenditures

H_{100}: CCI-1 is a significant predictor of two-year number of hospitalizations, controlling for age and sex.

$Model_{100}$: Two-year number of hospitalizations = age + sex + CCI-1

H_{101}: CCI-2 is a significant predictor of two-year number of hospitalizations, controlling for age and sex.

$Model_{101}$: Two-year number of hospitalizations = age + sex + CCI-2

H_{102}: CDS-1 is a significant predictor of two-year number of hospitalizations, controlling for age and sex.

$Model_{102}$: Two-year number of hospitalizations = age + sex + CDS-1

H_{103}: CDS-2 is a significant predictor of two-year number of hospitalizations, controlling for age and sex.

$Model_{103}$: Two-year number of hospitalizations = age + sex + CDS-2

H_{104}: Age, sex, the number of distinct medications, and index-year total healthcare expenditures together significantly predict two-year number of hospitalizations.

$Model_{104}$: Two-year total healthcare expenditures = age + sex + number of distinct medications + index-year number of hospitalizations

H_{105}: CCI-1 is a significant predictor of two-year number of hospitalizations, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{105}$: Two-year number of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1

H_{106}: CCI-2 is a significant predictor of two-year number of hospitalizations, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{106}$: Two-year number of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2

H_{107}: CDS-1 is a significant predictor of two-year number of hospitalizations, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{107}$: Two-year number of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-1

H_{108}: CDS-2 is a significant predictor of two-year number of hospitalizations, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{108}$: Two-year number of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-2

H_{109}: CDS-1 is a significant predictor of two-year number of hospitalizations, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{109}$: Two-year number of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-1

H_{110}: CDS-2 is a significant predictor of two-year number of hospitalizations, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{110}$: Two-year number of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-2

H_{111}: CDS-1 is a significant predictor of two-year number of hospitalizations, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{111}$: Two-year number of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-1

H_{112}: CDS-2 is a significant predictor of two-year number of hospitalizations, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{112}$: Two-year number of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-2

Two-Year Risk of Hospitalizations: Greater than or equal to one hospital admission in two years after the index period

H_{113}: Age and sex together significantly predict two-year risk of hospitalizations.

$Model_{113}$: Two-year risk of hospitalizations = age + sex

H_{114}: The number of distinct medications in the index period is a significant predictor of two-year risk of hospitalizations, controlling for age and sex.

$Model_{114}$: Two-year risk of hospitalizations = age + sex + number of distinct medications

H_{115}: The sum of total healthcare expenditures in the index period is a significant predictor of two-year risk of hospitalizations, controlling for age and sex.

$Model_{115}$: Two-year risk of hospitalizations = age + sex + index-year total healthcare expenditures

H_{116}: CCI-1 is a significant predictor of two-year risk of hospitalizations, controlling for age and sex.

$Model_{116}$: Two-year risk of hospitalizations = age + sex + CCI-1

H_{117}: CCI-2 is a significant predictor of two-year risk of hospitalizations, controlling for age and sex.

$Model_{117}$: Two-year total risk of hospitalizations = age + sex + CCI-2

H_{118}: CDS-1 is a significant predictor of two-year risk of hospitalizations, controlling for age and sex.

$Model_{118}$: Two-year risk of hospitalizations = age + sex + CDS-1

H_{119}: CDS-2 is a significant predictor of two-year risk of hospitalizations, controlling for age and sex.

$Model_{119}$: Two-year risk of hospitalizations = age + sex + CDS-2

H_{120}: Age, sex, the number of distinct medications, and index-year total healthcare expenditures together significantly predict two-year risk of hospitalizations.

$Model_{120}$: Two-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures

H_{121}: CCI-1 is a significant predictor of two-year risk of hospitalizations, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{121}$: Two-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1

H_{122}: CCI-2 is a significant predictor of two-year risk of hospitalizations, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{122}$: Two-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2

H_{123}: CDS-1 is a significant predictor of two-year risk of hospitalizations, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{123}$: Two-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-1

H_{124}: CDS-2 is a significant predictor of two-year risk of hospitalizations, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{124}$: Two-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-2

H_{125}: CDS-1 is a significant predictor of two-year risk of hospitalizations, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{125}$: Two-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-1

H_{126}: CDS-2 is a significant predictor of two-year risk of hospitalizations, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{126}$: Two-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-2

H_{127}: CDS-1 is a significant predictor of two-year risk of hospitalizations, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{127}$: Two-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-1

H_{128}: CDS-2 is a significant predictor of two-year risk of hospitalizations, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{128}$: Two-year risk of hospitalizations = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-2

One-Year Number of Emergency Department Visits

H_{129}: Age and sex together significantly predict one-year number of emergency department visits.

$Model_{129}$: One-year number of emergency department visits = age + sex

H_{130}: The number of distinct medications in the index period is a significant predictor of one-year number of emergency department visits, controlling for age and sex.

$Model_{130}$: One-year number of emergency department visits = age + sex + number of distinct medications

H_{131}: The sum of total healthcare expenditures in the index period is a significant predictor of one-year number of emergency department visits, controlling for age and sex.

$Model_{131}$: One-year number of emergency department visits = age + sex + index-year total healthcare expenditures

H_{132}: CCI-1 is a significant predictor of one-year number of emergency department visits, controlling for age and sex.

$Model_{132}$: One-year number of emergency department visits = age + sex + CCI-1

H_{133}: CCI-2 is a significant predictor of one-year number of emergency department visits, controlling for age and sex.

$Model_{133}$: One-year number of emergency department visits = age + sex + CCI-2

H_{134}: CDS-1 is a significant predictor of one-year number of emergency department visits, controlling for age and sex.

$Model_{134}$: One-year number of emergency department visits = age + sex + CDS-1

H_{135}: CDS-2 is a significant predictor of one-year number of emergency department visits, controlling for age and sex.

$Model_{135}$: One-year number of emergency department visits = age + sex + CDS-2

H_{136}: Age, sex, the number of distinct medications, and index-year total healthcare expenditures together significantly predict one-year number of emergency department visits.

$Model_{136}$: One-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures

H_{137}: CCI-1 is a significant predictor of one-year number of emergency department visits, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{137}$: One-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1

H_{138}: CCI-2 is a significant predictor of one-year number of emergency department visits, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{138}$: One-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2

H_{139}: CDS-1 is a significant predictor of one-year number of emergency department visits, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{139}$: One-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-1

H_{140}: CDS-2 is a significant predictor of one-year number of emergency department visits, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{140}$: One-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-2

H_{141}: CDS-1 is a significant predictor of one-year number of emergency department visits, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{141}$: One-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-1

H_{142}: CDS-2 is a significant predictor of one-year number of emergency department visits, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{142}$: One-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-2

H_{143}: CDS-1 is a significant predictor of one-year number of emergency department visits, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{143}$: One-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-1

H_{144}: CDS-2 is a significant predictor of one-year number of emergency department visits, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{144}$: One-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-2

One-Year Risk of Emergency Department Visits: Greater than or equal to one emergency department visit in one year after the index period

H_{145}: Age and sex together significantly predict one-year risk of emergency department visits.

$Model_{145}$: One-year risk of emergency department visits = age + sex

H_{146}: The number of distinct medications in the index period is a significant predictor of one-year risk of emergency department visits, controlling for age and sex.

$Model_{146}$: One-year risk of emergency department visits = age + sex + number of distinct medications

H_{147}: The sum of total healthcare expenditures in the index period is a significant predictor of one-year risk of emergency department visits, controlling for age and sex.

$Model_{147}$: One-year risk of emergency department visits = age + sex + index-year total healthcare expenditures

H_{148}: CCI-1 is a significant predictor of one-year risk of emergency department visits, controlling for age and sex.

$Model_{148}$: One-year risk of emergency department visits = age + sex + CCI-1

H_{149}: CCI-2 is a significant predictor of one-year risk of emergency department visits, controlling for age and sex.

$Model_{149}$: One-year total risk of emergency department visits = age + sex + CCI-2

H_{150}: CDS-1 is a significant predictor of one-year risk of emergency department visits, controlling for age and sex.

$Model_{150}$: One-year risk of emergency department visits = age + sex + CDS-1

H_{151}: CDS-2 is a significant predictor of one-year risk of emergency department visits, controlling for age and sex.

$Model_{151}$: One-year risk of emergency department visits = age + sex + CDS-2

H_{152}: Age, sex, the number of distinct medications, and index-year total healthcare expenditures together significantly predict one-year risk of emergency department visits.

$Model_{152}$: One-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures

H_{153}: CCI-1 is a significant predictor of one-year risk of emergency department visits, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{153}$: One-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1

H_{154}: CCI-2 is a significant predictor of one-year risk of emergency department visits, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{154}$: One-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2

H_{155}: CDS-1 is a significant predictor of one-year risk of emergency department visits, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{155}$: One-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-1

H_{156}: CDS-2 is a significant predictor of one-year risk of emergency department visits, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{156}$: One-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-2

H_{157}: CDS-1 is a significant predictor of one-year risk of emergency department visits, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{157}$: One-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-1

H_{158}: CDS-2 is a significant predictor of one-year risk of emergency department visits, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{158}$: One-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-2

H_{159}: CDS-1 is a significant predictor of one-year risk of emergency department visits, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{159}$: One-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-1

H_{160}: CDS-2 is a significant predictor of one-year risk of emergency department visits, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{160}$: One-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-2

Two-Year Number of Emergency Department Visits

H_{161}: Age and sex together significantly predict two-year number of emergency department visits.

$Model_{161}$: Two-year number of emergency department visits = age + sex

H_{162}: The number of distinct medications in the index period is a significant predictor of two-year number of emergency department visits, controlling for age and sex.

$Model_{162}$: Two-year number of emergency department visits = age + sex + number of distinct medications

H_{163}: The sum of total healthcare expenditures in the index period is a significant predictor of two-year number of emergency department visits, controlling for age and sex.

$Model_{163}$: Two-year number of emergency department visits = age + sex + index-year total healthcare expenditures

H_{164}: CCI-1 is a significant predictor of two-year number of emergency department visits, controlling for age and sex.

$Model_{164}$: Two-year number of emergency department visits = age + sex + CCI-1

H_{165}: CCI-2 is a significant predictor of two-year number of emergency department visits, controlling for age and sex.

$Model_{165}$: Two-year number of emergency department visits = age + sex + CCI-2

H_{166}: CDS-1 is a significant predictor of two-year number of emergency department visits, controlling for age and sex.

$Model_{166}$: Two-year number of emergency department visits = age + sex + CDS-1

H_{167}: CDS-2 is a significant predictor of two-year number of emergency department visits, controlling for age and sex.

$Model_{167}$: Two-year number of emergency department visits = age + sex + CDS-2

H_{168}: Age, sex, the number of distinct medications, and index-year total healthcare expenditures together significantly predict two-year number of emergency department visits.

$Model_{168}$: Two-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures

H_{169}: CCI-1 is a significant predictor of two-year number of emergency department visits, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{169}$: Two-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1

H_{170}: CCI-2 is a significant predictor of two-year number of emergency department visits, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{170}$: Two-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2

H_{171}: CDS-1 is a significant predictor of two-year number of emergency department visits, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{171}$: Two-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-1

H_{172}: CDS-2 is a significant predictor of two-year number of emergency department visits, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{172}$: Two-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-2

H_{173}: CDS-1 is a significant predictor of two-year number of emergency department visits, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{173}$: Two-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-1

H_{174}: CDS-2 is a significant predictor of two-year number of emergency department visits, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{174}$: Two-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-2

H_{175}: CDS-1 is a significant predictor of two-year number of emergency department visits, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{175}$: Two-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-1

H_{176}: CDS-2 is a significant predictor of two-year number of emergency department visits, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{176}$: Two-year number of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-2

Two-Year Risk of Emergency Department Visits: Greater than or equal to one emergency department visit in two years after the index period

H_{177}: Age and sex together significantly predict two-year risk of emergency department visits.

$Model_{177}$: Two-year risk of emergency department visits = age + sex

H_{178}: The number of distinct medications in the index period is a significant predictor of two-year risk of emergency department visits, controlling for age and sex.

$Model_{178}$: Two-year risk of emergency department visits = age + sex + number of distinct medications

H_{179}: The sum of total healthcare expenditures in the index period is a significant predictor of two-year risk of emergency department visits, controlling for age and sex.

$Model_{179}$: Two-year risk of emergency department visits = age + sex + index-year total healthcare expenditures

H_{180}: CCI-1 is a significant predictor of two-year risk of emergency department visits, controlling for age and sex.

$Model_{180}$: Two-year risk of emergency department visits = age + sex + CCI-1

H_{181}: CCI-2 is a significant predictor of two-year risk of emergency department visits, controlling for age and sex.

$Model_{181}$: Two-year total risk of emergency department visits = age + sex + CCI-2

H_{182}: CDS-1 is a significant predictor of two-year risk of emergency department visits, controlling for age and sex.

$Model_{182}$: Two-year risk of emergency department visits = age + sex + CDS-1

H_{183}: CDS-2 is a significant predictor of two-year risk of emergency department visits, controlling for age and sex.

$Model_{183}$: Two-year risk of emergency department visits = age + sex + CDS-2

H_{184}: Age, sex, the number of distinct medications, and index-year total healthcare expenditures together significantly predict two-year risk of emergency department visits.

$Model_{184}$: Two-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures

H_{185}: CCI-1 is a significant predictor of two-year risk of emergency department visits, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{185}$: Two-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1

H_{186}: CCI-2 is a significant predictor of two-year risk of emergency department visits, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{186}$: Two-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2

H_{187}: CDS-1 is a significant predictor of two-year risk of emergency department visits, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{187}$: Two-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-1

H_{188}: CDS-2 is a significant predictor of two-year risk of emergency department visits, controlling for age, sex, the number of distinct medications, and total healthcare expenditures in the index period.

$Model_{188}$: Two-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CDS-2

H_{189}: CDS-1 is a significant predictor of two-year risk of emergency department visits, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{189}$: Two-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-1

H_{190}: CDS-2 is a significant predictor of two-year risk of emergency department visits, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-1.

$Model_{190}$: Two-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-1 + CDS-2

H_{191}: CDS-1 is a significant predictor of two-year risk of emergency department visits, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{191}$: Two-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-1

H_{192}: CDS-2 is a significant predictor of two-year risk of emergency department visits, controlling for age, sex, the number of distinct medications, total healthcare expenditures in the index period, and the CCI-2.

$Model_{192}$: Two-year risk of emergency department visits = age + sex + number of distinct medications + index-year total healthcare expenditures + CCI-2 + CDS-2

Chapter 2 Methodology

This chapter discusses the methodology used for the study and consists of the following five sections: data source, study time frame, study sample, study design, and statistical analyses.

2.2 Data Source

This study used data from the Department of Defense TRICARE program's Military Health System Data Repository/Military Health System Management Analysis and Reporting Tool (MDR/M2) and the Pharmacy Data Transaction Service Data Warehouse (PDTS). The MDR/M2 contains claims for medical services through: 1) military direct inpatient care (Standard Inpatient Data Record); 2) military direct outpatient care (Standard Ambulatory Data Record); 3) managed care inpatient services (TRICARE Encounter Data Institutionalized); and 4) managed care outpatient services (TRICARE Encounter Data Non-institutionalized). The PDTS supplies prescription data directly to the MDR/M2 and contains prescription claims for all three points of service (military pharmacies, mail-order pharmacies, community pharmacies). Table 2.1 describes the data fields retrieved from MDR/M2 and PDTS.

Table 2.1: Descriptions of Data Fields from the TRICARE Military Health System (MHS) Data Repository/MHS Management Analysis and Reporting Tool and the Pharmacy Data Transaction Service (PDTS) Data Warehouse

Data Field	**Description of Data Field**
From *Cohort* data file (containing patient demographic information)	
EDIPN	Patient unique identifier
DOB	Date of birth
Sex	Sex
ACV	Alternate Care Value, indicating type of TRICARE enrollment of the beneficiary
BENCATCOM	Beneficiary Category Common, indicating beneficiary categories
HSSCREG	Beneficiary Health Services and Support Contract region, indicating the HSSC region of the beneficiary zip code
From *Standard Inpatient Data Record* file	
EDIPN	Patient unique identifier
MTF	Medical treatment facility
PRN	Patient record number
FY	Fiscal year based on disposition date
DX1-DX20	First through twentieth ICD-9 diagnosis code
PROC1-PROC20	First through twentieth ICD-9 procedure code
ADMDATE	Admission date
DISPDATE	Disposition date
DISPTYPE	Disposition status
DMISDAYS	Total bed days
FULLCOST	Full cost (the sum of medical, pharmacy, laboratory, and radiology costs plus payments by TRICARE, patients, and other insurers)
FCANCLAB	Ancillary laboratory portion of full cost
FCANCRAD	Ancillary radiology portion of full cost
From *TRICARE Encounter Data Institutionalized* file	
EDIPN	Patient unique identifier
TEDNO	TRICARE Encounter Data number
INSTTYPE	Type of institution
ACUTE	Acute care hospital indicator
FY	Fiscal year based on disposition date
DX1-DX12	First through twelfth ICD-9 diagnosis code
PROC1-PROC12	First through twelfth ICD-9 procedure code
ADMTYPE	Admission type
ADMDATE	Admission date
BEGDATE	Begin date of care
ENDDATE	End date of care
DISPTYPE	Disposition status
TOTDAYS	Total bed days

Table 2.1 (Continued)

Data Field	**Description of Data Field**
PAID	Total amount paid by TRICARE
OHI	Total amount paid by other health insurance
PATCOST	Total amount paid by patient
From *Standard Ambulatory Data Record* file	
EDIPN	Patient unique identifier
APPTIDNO	Appointment identification number
DMISID	Defense Medical Information System identifier for treatment
FY	Fiscal year based on disposition date
ER	Emergency department use identifier
ENCDATE	Encounter date
DISPCODE	Disposition code
ICD1-ICD4	First through fourth ICD-9 diagnosis code
CPT1-CPT10	First through tenth CPT (Current Procedure Terminology) code
FCOST	Full cost (the sum of medical, pharmacy, laboratory, and radiology costs plus payments by TRICARE, patients, and other insurers)
FCLAB	Full laboratory cost (laboratory portion of full cost)
FCRAD	Full radiology cost (radiology portion of full cost)
FCRX	Full pharmacy cost (pharmacy portion of full cost)
From *TRICARE Encounter Data Non-institutionalized* file	
EDIPN	Patient unique identifier
TEDNO	TRICARE Encounter Data number
LINUM	Line item number
FY	Fiscal year based on disposition date
ERVIS	Emergency department visit identifier
DX1-DX8	First through eighth ICD-9 diagnosis code
PAID	Total amount paid by TRICARE
OHI	Total amount paid by other health insurance
PATCOST	Total amount paid by patient
BEGDATE	Begin date of care
ENDDATE	End date of care
CPT	Current Procedure Terminology code
PLACE	Place of service
From *Pharmacy Data Transaction Service Data Warehouse* file	
EDIPN	Patient unique identifier
FY	Fiscal year
DATEDISP	Date dispensed
AUTHNUM	Authorization number
GCN	Generic code number
NDC	National drug code
AHFS	American Hospital Formulary Service code

Table 2.1 (Continued)

Data Field	**Description of Data Field**
RXNAME	Product name
DAYS	Days supply
ICOST	Ingredient cost
GAMT	Sub gross amount
COPAY	Sub copay amount
OHI	Amount paid by other health insurance
FILLOC	Fill location
From *Laboratory/Ancillary* data file	
EDIPN	Patient unique identifier
FY	Fiscal year
FULLCOST	Full cost
RECTYPE	Record type
SERVDATE	Service date

2.3 STUDY TIME FRAME

This study used inpatient and outpatient claims data from October 1, 2005 to September 30, 2008.

2.4 STUDY SAMPLE

Eligible patients in the MDR/M2 database were identified using the following inclusion and exclusion criteria.

Inclusion criteria:

1. The patient had a diagnosis of diabetes (ICD-9-CM code 250.xx) using inpatient or outpatient services and at least one prescription claim for oral antidiabetic medication, insulin, or incretin mimetic between October 1, 2005 and September 30, 2006.

2. The patient was a non-active duty beneficiary continuously enrolled in the TRICARE Prime program for at least 10 of 12 months in each fiscal year from October 1, 2005 to September 30, 2008.

Exclusion criteria:

1. A female patient who had a prescription for prenatal vitamins anytime during the study period because she might have gestational diabetes.
2. A patient who was born on or before September 30, 1943 (i.e., over 65 years of age at the end of the study period) because the patient might have received care through Medicare.
3. A patient who received care outside the CONUS service area (i.e., 50 states, the District of Columbia, Puerto Rico, Guam and the U.S. Virgin Islands) at any time during the study period because records on healthcare expenditures may be incomplete.

The final study sample consisted of approximately 10 percent of randomly selected sample of patients who met the inclusion and exclusion criteria.

2.5 STUDY DESIGN

This study was a retrospective cohort analysis. Patients were selected to enter the cohort based on the inclusion and exclusion criteria. Subjects were censored at the end of the study period. The fiscal year 2006 (October 1, 2005 to September 30, 2006) was set as the index year to identify age, sex, ambulatory encounters, and inpatient encounters, which were then used to calculate the index-period total healthcare expenditures, number

of distinct medications, the CCI scores, and the CDS scores. Healthcare utilization (i.e., emergency department visits, hospitalizations) and expenditures were identified for fiscal years 2007 and 2008.

2.5.1 Comorbidity Assessment

Six different comorbidity adjustment measures were assessed:

The number of distinct medications in the index year was calculated as the sum of unique medications used. If two drugs had different doses but the same active ingredient, they were considered to be one unique medication.

Index-year total healthcare expenditures were calculated as the sum of amounts paid by TRICARE, other health insurance, and the patient for ambulatory visits, hospitalizations, emergency department visits, laboratory tests, radiological studies, and pharmaceuticals.

Two adaptations of the CCI were used: the Deyo adaption (CCI-1) and Charlson et al.'s 2008 adaptation (CCI-2). Based on CCI-1, diagnoses were identified through ICD-9 codes and assigned weights of one, two, three, or six to obtain a summary score for each individual patient. Since the CCI-2 also bases its derivation on the CCI-1 coding scheme, the 19 original diagnoses were identified as described in CCI-1, while the three additional diagnoses (i.e., depression, hypertension, skin ulcers and cellulitis) were identified through their corresponding ICD-9 codes, and the use of warfarin was identified using the pharmacy prescription claims. All patients had a minimum CCI-1 or CCI-2 score of one because they had a diagnosis of diabetes.

Both Von Korff et al.'s CDS version (CDS-1) and Clark et al.'s CDS version (CDS-2) were used. For CDS-1, a summary integer score was produced based on the patient's medication use. The CDS-2 includes more chronic conditions and medication classes than CDS-1 and presents three different sets of weights for prediction of total cost, outpatient cost, and primary care visits, respectively. For this study, the regression weights for total cost were used based on the developers' recommendation.[96] Medications that became available since 1992 were included in the calculation of scores if they were used to treat chronic conditions listed in the CDS-1 and CDS-2. Classification of drugs was based on the American Hospital Formulary Service (AHFS) codes, generic code numbers (GCNs), or drug names.

2.5.2 Post-index Utilization Measures

The cohort was followed up for two years to determine healthcare utilization and expenditures including: 1) total healthcare expenditures, 2) high-expenditure individuals, 3) number of hospitalizations, 4) risk of hospitalizations, 5) number of emergency department visits, and 6) risk of emergency department visits.

Post-index total healthcare expenditures were calculated as the sum of amounts paid by TRICARE, other health insurance, and the patient for ambulatory visits, hospitalizations, emergency department visits, laboratory tests, radiological studies, and pharmaceuticals. For total healthcare expenditures, a 90^{th} percentile was ascertained to

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[96] Clark et al., "A Chronic Disease Score with Empirically Derived Weights."

divide the patients into a high-expenditure group (≥ 90th percentile) and a low-expenditure group (< 90th percentile).[97]

The number of hospitalizations was calculated as the sum of inpatient admissions for any cause with total bed days equal to or more than one. The disposition date was used to determine in which fiscal year the hospitalization occurred. The risk of hospitalizations was defined as having one or more hospitalizations during the follow-up period.

The number of emergency department visits was calculated as the sum of visits to the emergency department for any cause. The discharge date was used to determine in which fiscal year the emergency department visit occurred. The risk of emergency department visits was defined as having one or more emergency department visits during the follow-up period.

2.6 Statistical Analyses

Descriptive statistics were calculated to examine the means, standard deviations, and distributions of demographics, healthcare utilization, and comorbidities of the patients. The predictive performance of the models was first examined by regressing the dependent variables on each set of predictors in multivariate linear regression models. An R^2 statistic was produced from each regression model, representing the amount of variation in the dependent variable explained by the set of predictors. A higher R^2 value

[97] Farley, Harley, and Devine, "A Comparison of Comorbidity Measurements to Predict Healthcare Expenditures."

indicates better overall prediction power, and vice versa. Thus, each model's relative predictive performance may be ranked accordingly.

Logistic regression analyses were conducted to examine model discrimination and calibration. For each logistic regression model, a *c* statistic was calculated, representing the area under curve of the receiver-operator characteristic (ROC). The ROC curves take into account correlations resulting from using the same sample of individuals,[98] and are graphically presented as a plot of sensitivity and one minus specificity for all discrimination values of a predictor. Ideally, a predictor should be constructed in such a way that it could successfully identify true positive cases (i.e., sensitivity) while avoiding false positive cases (i.e., one minus specificity). A *c* statistic of 0.5 indicates no predictive ability because it is equivalent to random prediction; a *c* statistic of 1.0 indicates perfect prediction. The discriminating power of prediction models was tested by comparing the magnitudes of the *c* statistics.

The Hosmer-Lemeshow goodness-of-fit chi-square test was conducted to examine the calibration of each logistic regression model. The test compares the observed and predicted number of cases of an outcome across a number of groups.[99] In this study, the level of risk was categorized into deciles to test the calibration curves of the predictor models. If the distribution of predicted cases aligns well with the distribution of observed cases, then the model demonstrates good calibration, indicated by a low chi-square value.

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[98] Elizabeth R. DeLong, David M. DeLong, and Daniel L. Clarke-Pearson, "Comparing the Areas under Two or More Correlated Receiver Operating Characteristic Curves: A Nonparametric Approach," *Biometrics* 44, no. 3 (1988).

[99] Stanley Lemeshow and David W. Hosmer Jr., "A Review of Goodness of Fit Statistics for Use in the Development of Logistic Regression Models," *American Journal of Epidemiology* 115, no. 1 (1982).

Conversely, a higher chi-square value (i.e., a smaller p value) indicates poorer model fit and calibration.

All statistical analyses were conducted using SAS®, and a *p* value of less than 0.05 was considered statistically significant.

Chapter 3 Results

This chapter presents the results from the analyses and consists of the following four sections: 1) descriptive statistics on the study sample, 2) modeling results on the prediction of total healthcare expenditures, 3) modeling results on the prediction of hospitalizations, and 4) modeling results on the prediction of emergency department visits.

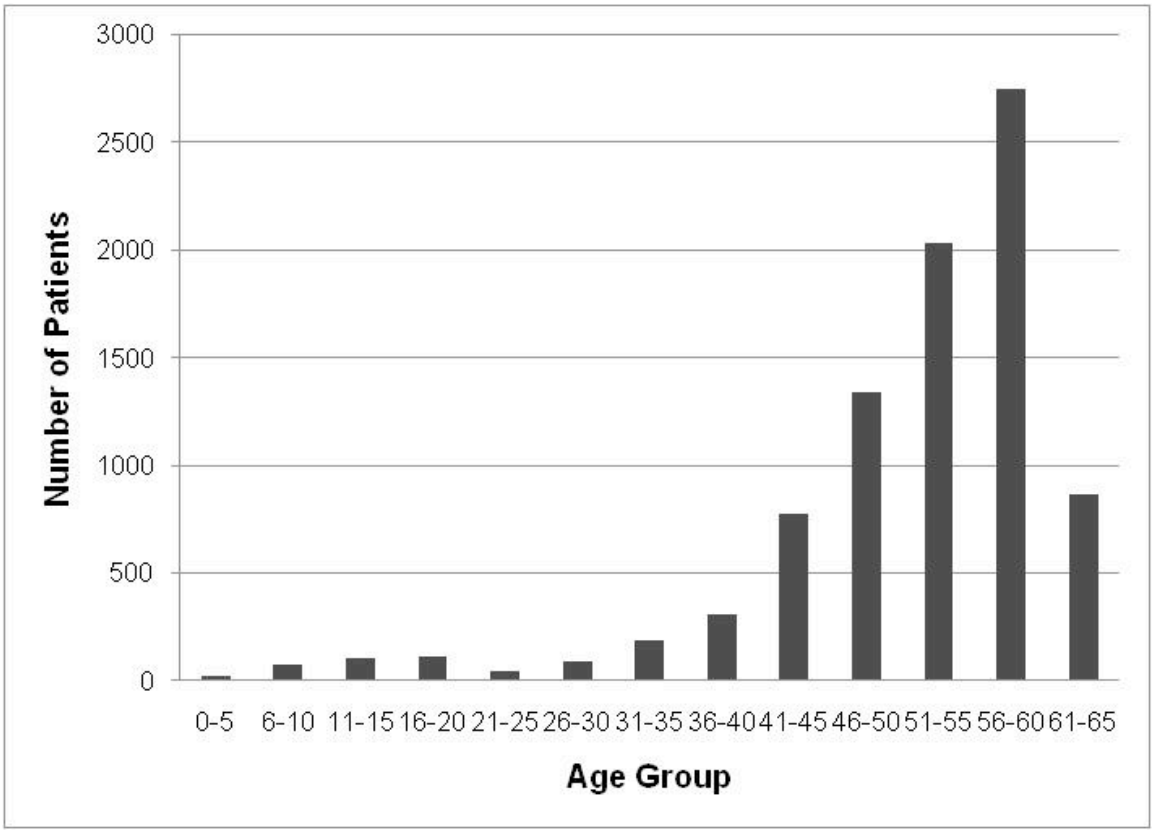
3.1 Department of Defense TRICARE Study Sample

The Department of Defense Pharmacoeconomic Center prescreened and randomly selected a sample of 9,000 patients meeting the study inclusion and exclusion criteria. Further examination of the claims records eliminated 295 patients who did not have a valid diabetes diagnosis in the index year and one patient whose sex was coded inaccurately. Therefore, the final study sample included 8,704 Department of Defense TRICARE beneficiaries with diabetes, including military personnel, retirees, and their dependents. All 8,704 patients had at least one inpatient or outpatient diagnosis of diabetes and at least one prescription claim for oral antidiabetic medication, insulin, or incretin mimetic between October 1, 2005 and September 30, 2006. All patients were under the age of 65, on non-active duty, and continuously enrolled in the TRICARE Prime program for at least 10 of 12 months in each fiscal year from October 1, 2005 to September 30, 2008. Patients were excluded if they received care outside the CONUS service area (i.e., 50 states, the District of Columbia, Puerto Rico, Guam and the U.S.

Virgin Islands) at any time during the study period. Patients were also excluded if they were female and had a prescription for prenatal vitamins during the study.

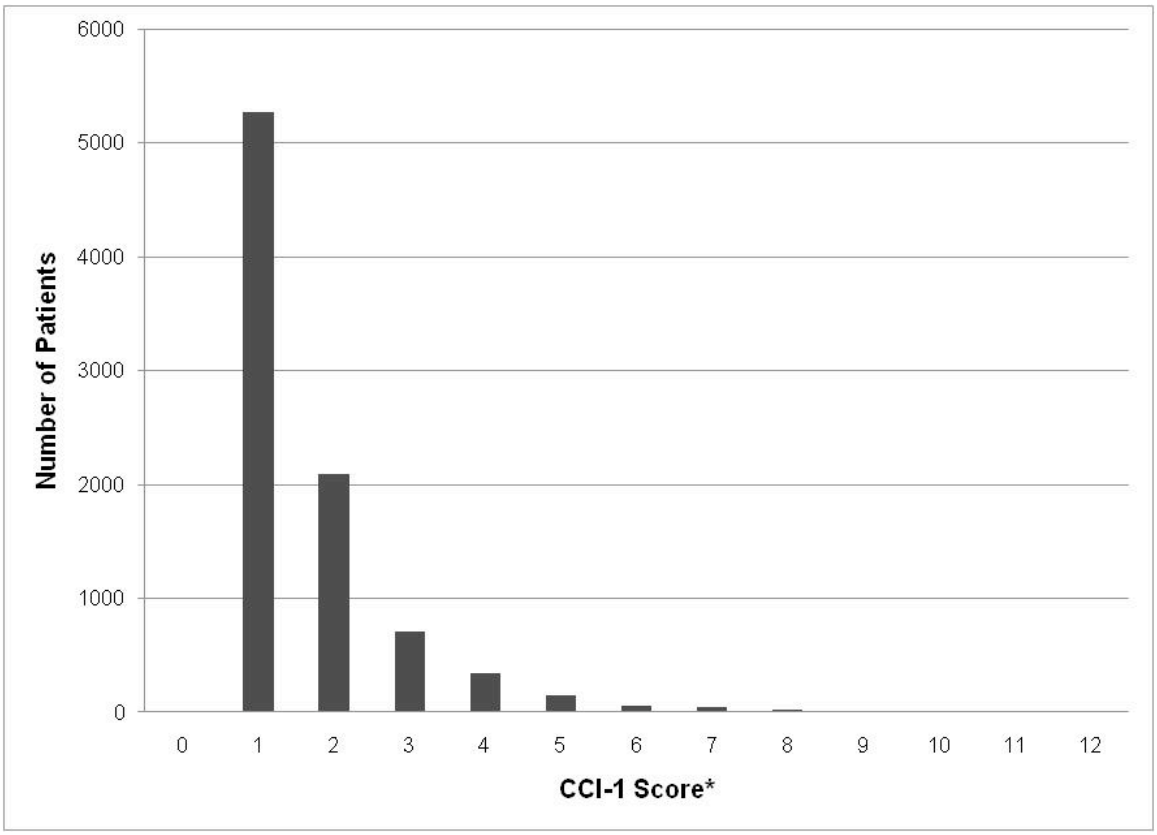
Of the 8,704 patients, 4,674 (53.7%) were females and 4,030 (46.3%) were males. The mean (SD) age of the sample was 51.0 (10.5) years. The mean (SD) index-year total healthcare expenditures were $10,333 ($28,131), with a minimum of $119 and a maximum of $956,657. The mean (SD) index-year number of distinct medications was 12.8 (7.3), with a minimum of one and a maximum of 65. Figure 3.1 shows the patient distribution by five-year age groups.

Figure 3.1: Patient Sample by Age Group (N=8,704)



The mean (SD) CCI-1 score in the study sample was 1.7 (1.2); the minimum was one and the maximum was 12. Figure 3.2 shows the distribution of the CCI-1 scores.

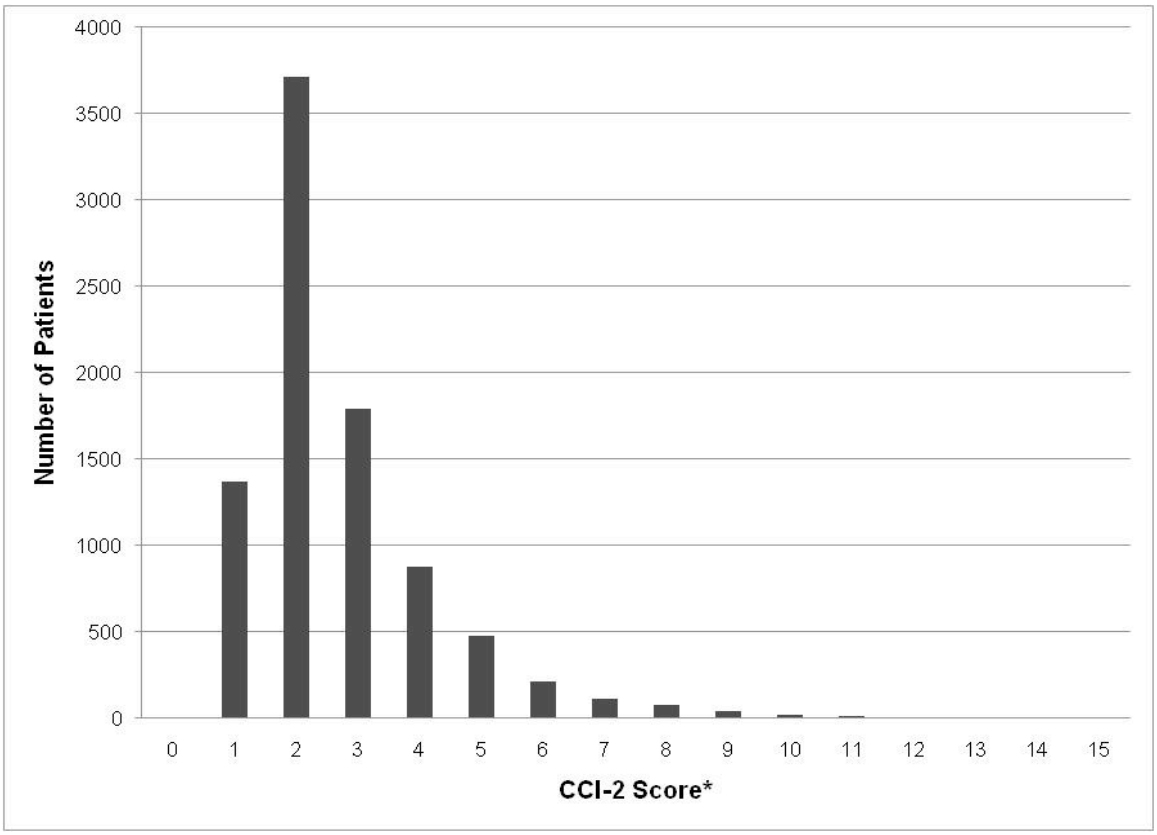
Figure 3.2: Distribution of the Charlson Comorbidity Index – Deyo adaptation (CCI-1) Scores in the Study Sample (N=8,704)



* The scores were derived using Deyo et al.'s adaptation: Deyo RA, Cherkin DC, and Ciol MA. "Adapting a Clinical Comorbidity Index for Use with ICD-9-CM Administrative Databases." *Journal of Clinical Epidemiology* 45, (1992): 613-19.

The mean (SD) CCI-2 score in the study sample was 2.7 (1.5); the minimum was one and the maximum was 15. Figure 3.3 shows the distribution of the CCI-2 scores.

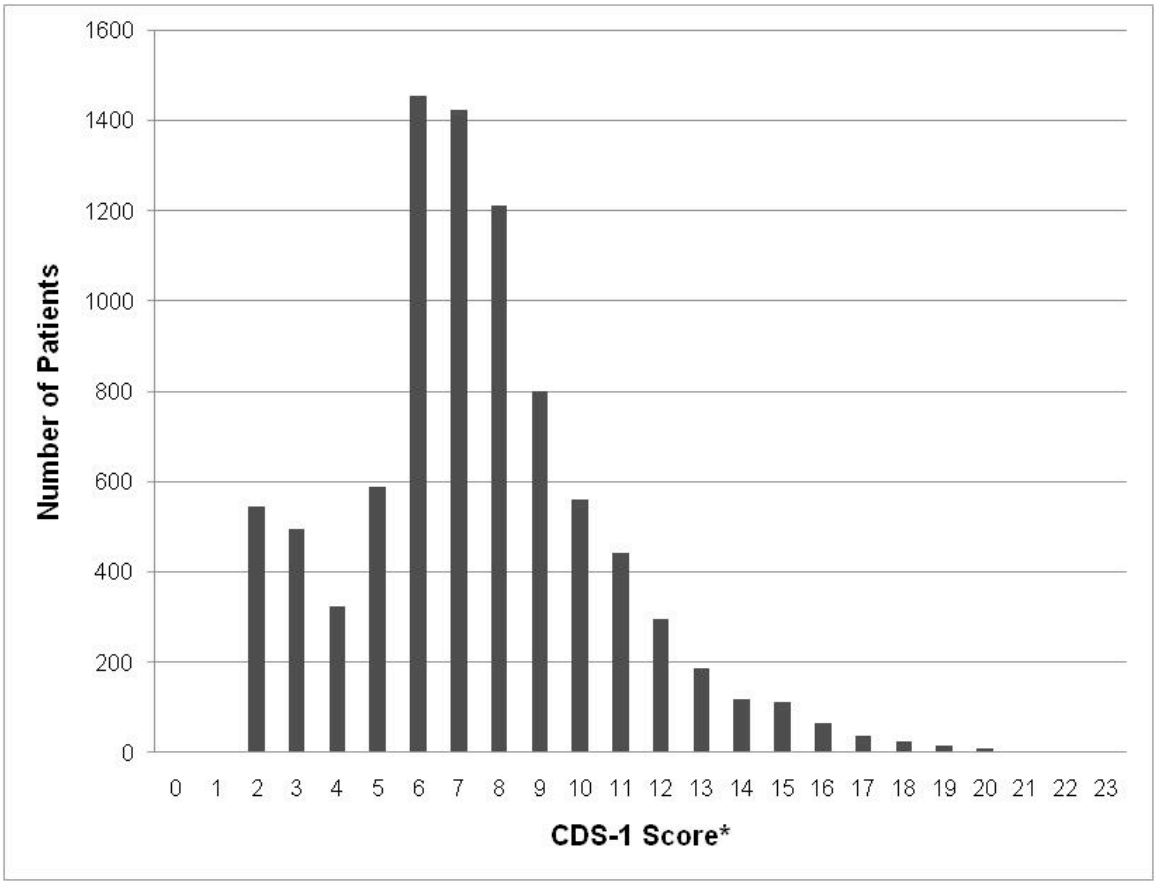
Figure 3.3: Distribution of the Charlson Comorbidity Index – 2008 version (CCI-2) Scores in the Study Sample (N=8,704)



* The scores were derived using Charlson et al.'s 2008 version: Charlson ME, Charlson RE, Peterson JC, et al. "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients." Journal of Clinical Epidemiology 61, no. 12 (2008): 1234-40.

The mean (SD) CDS-1 score in the study sample was 7.4 (3.1); the minimum was two and the maximum was 23. Figure 3.4 shows the distribution of the CDS-1 scores.

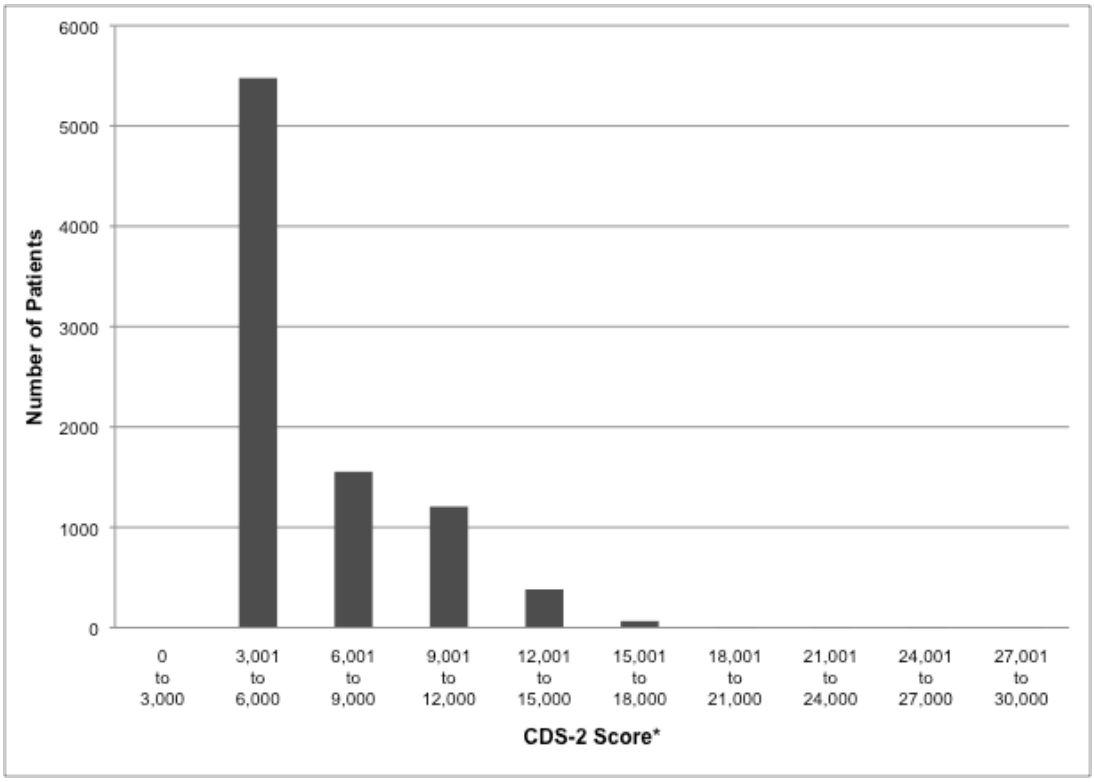
Figure 3.4 Distribution of the Chronic Disease Score – Von Korff Version (CDS-1) Scores in the Study Sample (N=8,704)



* The scores were derived based on: Von Korff M, Wagner EH, and Saunders K. "A Chronic Disease Score from Automated Pharmacy Data." Journal of Clinical Epidemiology 45, no. 2 (1992): 197-203

The mean (SD) CDS-2 score in the study sample was 6,150 (3,012); the minimum was 3,046 and the maximum was 28,230. Figure 3.5 shows the distribution of the CDS-2 scores.

Figure 3.5: Distribution of the Chronic Disease Score – Clark Version (CDS-2) Scores in the Study Sample (N=8,704)



*

The scores were derived based on: Clark DO, von Korff M, Saunders K, et al. "A Chronic Disease Score with Empirically Derived Weights." Medical Care 33, no. 8 (1995): 783-95.

Descriptive statistics on healthcare utilization and expenditures in the post-index one-year and two-year periods are presented in Table 3.1.

Table 3.1: Total Healthcare Expenditures, Number of Hospitalizations, and Number of Emergency Department Visits for Diabetic Patients in One Year and Two Years Post-Index

N=8,704	Mean	Standard Deviation	Median	90th Percentile	Minimum	Maximum
Total Healthcare Expenditures						
1 Year Post-Index	$10,750	$26,661	$5,196	$21,711	$0	$959,359
2 Years Post-Index	$22,991	$50,522	$12,054	$45,323	$0	$1,721,847
Number of Hospitalizations						
1 Year Post-Index	0.2	0.7	0	1	0	12
2 Years Post-Index	0.4	1.2	0	1	0	19
Number of Emergency Department Visits						
1 Year Post-Index	0.6	1.3	0	2	0	30
2 Years Post-Index	1.2	2.2	0	3	0	50

In the post-index one-year period, 871 patients had healthcare expenditures higher than $21,711 (i.e., 90th percentile), 1,177 patients had at least one hospital admission, and 2,747 patients had at least one visit to the emergency department. In the post-index two-year period, 871 patients had healthcare expenditures higher than $45,323 (90th percentile), 2,029 patients had at least one hospital admission, and 4,165 patients had at least one visit to the emergency department.

3.2 Modeling Results: Prediction of Total Healthcare Expenditures

3.2.1 One-year Total Healthcare Expenditures – Linear Regression Models:

Controlling for age and sex, all six predictors produced significant increases of variance explained in one-year total healthcare expenditures: the number of distinct medications added an additional 7.2% of the variance ($F = 681.0$; $df = 1, 8700$; $p < .0001$); the index-year total healthcare expenditures added an additional 35.4% of the variance ($F = 4778.9$; $df = 1, 8700$; $p < .0001$); CCI-1 added an additional 11.0% of the variance ($F = 1079.8$; $df = 1, 8700$; $p < .0001$); CCI-2 added an additional 11.3% of the variance ($F = 1110.9$; $df = 1, 8700$; $p < .0001$); CDS-1 added an additional 3.6% of the variance ($F = 329.4$; $df = 1, 8700$; $p < .0001$); and CDS-2 added an additional 5.3% of the variance ($F = 487.7$; $df = 1, 8700$; $p < .0001$).

Controlling for age, sex, number of distinct medications, and index-year total healthcare expenditures, the four comorbidity adjustment measures contributed significant proportions of the variance in one-year total healthcare expenditures: including CCI-1 increased the variance explained by 0.8% ($F = 112.1$; $df = 1, 8698$; $p < .0001$); including CCI-2 increased the variance explained by 0.5% ($F = 74.2$; $df = 1, 8698$; $p < .0001$); including CDS-1 increased the variance explained by 0.03% ($F = 4.6$; $df = 1, 8698$; $p = .032$); and including CDS-2 increased the variance explained by 0.03% ($F = 5.6$; $df = 1, 8698$; $p = .018$).

Controlling for age, sex, number of distinct medications, index-year total healthcare expenditures, and CCI-1, neither CDS-1 ($\Delta R^2 = 0.0\%$; $F = 0.5$; $df = 1, 8697$; p

= .46) nor CDS-2 (ΔR^2 = 0.0%; F = 0.8; df = 1, 8697; p = .37) explained a significant proportion of the variance in one-year healthcare expenditures.

Controlling for age, sex, number of distinct medications, index-year total healthcare expenditures, and CCI-2, neither CDS-1 (ΔR^2 = 0.0%; F = 0.4; df = 1, 8697; p = .53) nor CDS-2 (ΔR^2 = 0.01%; F = 2.0; df = 1, 8697; p = .16) explained a significant portion of the variance in one-year healthcare expenditures.

Table 3.2.1 summarizes the results from section 3.2.1.

Table 3.2.1: Linear Regression Modeling Results: Prediction of Total Healthcare Expenditures in the One-Year Post-Index Period

Models			**R^2 Difference Tests**			
No.	Predictors	Adj. R^2 (%)	ΔR^2 (%)	F value	d.f.	*p* value
			Baseline model: model 1			
1	Age + Sex	0.26	--	--	--	--
2	Age + Sex + # of Meds	7.49	7.23	681.0	1, 8700	< 0.0001
3	Age + Sex + Index-year Expenditures	35.62	35.36	4778.9	1, 8700	< 0.0001
4	Age + Sex + CCI-1	11.26	11.00	1079.8	1, 8700	< 0.0001
5	Age + Sex + CCI-2	11.54	11.28	1110.9	1, 8700	< 0.0001
6	Age + Sex + CDS-1	3.89	3.63	329.4	1, 8700	< 0.0001
7	Age + Sex + CDS-2	5.54	5.28	487.7	1, 8700	< 0.0001
			Baseline model: model 8			
8	Age + Sex + # of Meds + Index-year Expenditures	36.43	--	--	--	--
9	Age + Sex + # of Meds + Index-year Expenditures + CCI-1	37.23	0.80	112.1	1, 8698	< 0.0001
10	Age + Sex + # of Meds + Index-year Expenditures + CCI-2	36.96	0.53	74.2	1, 8698	< 0.0001
11	Age + Sex + # of Meds + Index-year Expenditures + CDS-1	36.46	0.03	4.6	1, 8698	0.032
12	Age + Sex + # of Meds + Index-year Expenditures + CDS-2	36.46	0.03	5.6	1, 8698	0.018
			Baseline model: model 9			
13	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-1	37.23	0.00	0.5	1, 8697	0.46
14	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-2	37.23	0.00	0.8	1, 8697	0.37
			Baseline model: model 10			
15	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-1	36.96	0.00	0.4	1, 8697	0.53
16	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-2	36.97	0.01	2.0	1, 8697	0.16

# of Meds: number of distinct medications; Adj. R^2: adjusted R^2 ; ΔR^2 : difference in R^2 ; d.f.: degrees of freedom

CCI-1 is based on Deyo RA, et al. "Adapting a Clinical Comorbidity Index for Use with ICD-9-CM Administrative Databases." *Journal of Clinical Epidemiology* 45, (1992): 613-19.

CCI-2 is based on Charlson ME, et al. "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients." *Journal of Clinical Epidemiology* 61, no. 12 (2008): 1234-40.

CDS-1 is based on Von Korff M, et al. "A Chronic Disease Score from Automated Pharmacy Data." *Journal of Clinical Epidemiology* 45, no. 2 (1992): 197-203.

CDS-2 is based on Clark DO, et al. "A Chronic Disease Score with Empirically Derived Weights." *Medical Care* 33, no. 8 (1995): 783-95.

3.2.2 One-year High Healthcare Expenditures – Logistic Regression Models:

In predicting one-year high (≥ 90th percentile) healthcare expenditures, the index-year healthcare expenditures had the highest predictive power (*c* = .810), followed by the number of distinct medications (*c* = .767), CCI-2 (*c* = .749), CDS-2 (*c* = .737), CCI-1 (*c* = .735), and CDS-1 (*c* = .719), where age and sex were included in the models. Results from the Hosmer-Lemeshow goodness-of-fit tests indicated good model fit only for the model that included the number of distinct medications (χ^2 = 4.8; df = 8; p = .78) but poor model fits for the models that included the index-year total healthcare expenditures (χ^2 = 141.9; df = 8; p < .0001), CCI-1 (χ^2 = 26.1; df = 8; p = .0010), CCI-2 (χ^2 = 16.0; df = 8; p = .042), CDS-1 (χ^2 = 28.1; df = 8; p = .0005), and CDS-2 (χ^2 = 58.3; df = 8; p < .0001).

With the inclusion of age, sex, number of distinct medications, and index-year total healthcare expenditures in the models, adding the CCI-1 or CCI-2 produced the same predictive power (*c* = .813). With the inclusion of age, sex, number of distinct medications, and index-year total healthcare expenditures in the models, adding the CDS-1 or CDS-2 produced similar predictive power (*c* = .808 for CDS-1; *c* = .809 for CDS-2). Results from the Hosmer-Lemeshow goodness-of-fit tests indicated good model fit for the models that included the CCI-1 (χ^2 = 10.7; df = 8; p = .22), CCI-2 (χ^2 = 10.5; df = 8; p = .23), and CDS-1 (χ^2 = 10.6; df = 8; p = .23); however, the fit was poor for the model that included the CDS-2 (χ^2 = 21.7; df = 8; p = .0054)

The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-1, and CDS-1 produced a *c* statistic of .813, with good

model fit (χ^2 = 9.0; df = 8; p = .35). The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-1, and CDS-2 produced a *c* statistic of .814, with good model fit (χ^2 = 9.5; df = 8; p = .30).

The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-2, and CDS-1 produced a *c* statistic of .812, with good model fit (χ^2 = 9.9; df = 8; p = .27). The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-2, and CDS-2 produced a *c* statistic of .813, with good model fit (χ^2 = 12.1; df = 8; p = .15).

Table 3.2.2 summarizes the results from section 3.2.2.

Table 3.2.2: Logistic Regression Modeling Results: Prediction of High (≥ 90th Percentile) Healthcare Expenditures in the One-Year Post-Index Period

Models			Hosmer-Lemeshow Tests		
No.	Predictors	*c* statistic	χ^2	d.f.	*p* value
17	Age + Sex	0.575	4.7	8	0.79
18	Age + Sex + # of Meds	0.767	4.8		0.78
19	Age + Sex + Index-year Expenditures	0.810	141.9		< 0.0001
20	Age + Sex + CCI-1	0.735	26.1		0.0010
21	Age + Sex + CCI-2	0.749	16.0		0.042
22	Age + Sex + CDS-1	0.719	28.1		0.0005
23	Age + Sex + CDS-2	0.737	58.3		< 0.0001
24	Age + Sex + # of Meds + Index-year Expenditures	0.807	11.7		0.16
25	Age + Sex + # of Meds + Index-year Expenditures + CCI-1	0.813	10.7		0.22
26	Age + Sex + # of Meds + Index-year Expenditures + CCI-2	0.813	10.5		0.23
27	Age + Sex + # of Meds + Index-year Expenditures + CDS-1	0.808	10.6		0.23
28	Age + Sex + # of Meds + Index-year Expenditures + CDS-2	0.809	21.7		0.0054
29	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-1	0.813	9.0		0.35
30	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-2	0.814	9.5		0.30
31	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-1	0.812	9.9		0.27
32	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-2	0.813	12.1		0.15

# of Meds: number of distinct medications; d.f.: degrees of freedom

CCI-1 is based on Deyo RA, et al. "Adapting a Clinical Comorbidity Index for Use with ICD-9-CM Administrative Databases." *Journal of Clinical Epidemiology* 45, (1992): 613-19.

CCI-2 is based on Charlson ME, et al. "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients." *Journal of Clinical Epidemiology* 61, no. 12 (2008): 1234-40.

CDS-1 is based on Von Korff M, et al. "A Chronic Disease Score from Automated Pharmacy Data." *Journal of Clinical Epidemiology* 45, no. 2 (1992): 197-203.

CDS-2 is based on Clark DO, et al. "A Chronic Disease Score with Empirically Derived Weights." *Medical Care* 33, no. 8 (1995): 783-95.

3.2.3 Two-year Total healthcare Expenditures – Linear Regression Models:

Controlling for age and sex, all six predictors produced significant increases of variance explained in two-year total healthcare expenditures: the number of distinct medications added an additional 8.0% of the variance ($F = 757.6$; $df = 1, 8700$; $p < .0001$); the index-year total healthcare expenditures added an additional 31.2% of the variance ($F = 3971.6$; $df = 1, 8700$; $p < .0001$); CCI-1 added an additional 11.7% of the variance ($F = 1152.2$; $df = 1, 8700$; $p < .0001$); CCI-2 added an additional 12.0% of the variance ($F = 1191.1$; $df = 1, 8700$; $p < .0001$); CDS-1 added an additional 4.1% of the variance ($F = 370.6$; $df = 1, 8700$; $p < .0001$); and CDS-2 added an additional 5.7% of the variance ($F = 529.5$; $df = 1, 8700$; $p < .0001$).

Controlling for age, sex, number of distinct medications, and index-year total healthcare expenditures, the four comorbidity adjustment measures contributed significant proportions of the variance in two-year total healthcare expenditures: including CCI-1 increased the variance explained by 1.2% ($F = 154.3$; $df = 1, 8698$; $p < .0001$); including CCI-2 increased the variance explained by 0.8% ($F = 110.8$; $df = 1, 8698$; $p < .0001$); including CDS-1 increased the variance explained by 0.04% ($F = 5.7$; $df = 1, 8698$; $p = .017$); and including CDS-2 increased the variance explained by 0.05% ($F = 7.5$; $df = 1, 8698$; $p = .063$).

Controlling for age, sex, number of distinct medications, index-year total healthcare expenditures, and CCI-1, neither CDS-1 ($\Delta R^2 = 0.0\%$; $F = 0.5$; $df = 1, 8697$; p

= .46) nor CDS-2 (ΔR^2 = 0.0%; F = 1.0; df = 1, 8697; p = .31) explained a significant portion of the variance in two-year healthcare expenditures.

Controlling for age, sex, number of distinct medications, index-year total healthcare expenditures, and CCI-2, neither CDS-1 (ΔR^2 = -0.01%; F = 0.3; df = 1, 8697; p = .59) nor CDS-2 (ΔR^2 = 0.0%; F = 2.5; df = 1, 8697; p = .11) explained a significant portion of the variance in two-year healthcare expenditures.

Table 3.2.3 summarizes the results from section 3.2.3.

Table 3.2.3: Linear Regression Modeling Results: Prediction of Total Healthcare Expenditures in the Two-Year Post-Index Period

Models			**R^2 Difference Tests**			
No.	Predictors	Adj. R^2 (%)	ΔR^2 (%)	F value	d.f.	*p* value
			Baseline model: model 33			
33	Age + Sex	0.32	--	--	--	--
34	Age + Sex + # of Meds	8.29	7.97	757.6	1, 8700	< 0.0001
35	Age + Sex + Index-year Expenditures	31.55	31.23	3971.0	1, 8700	< 0.0001
36	Age + Sex + CCI-1	11.97	11.65	1152.2	1, 8700	< 0.0001
37	Age + Sex + CCI-2	12.31	11.99	1191.1	1, 8700	< 0.0001
38	Age + Sex + CDS-1	4.38	4.06	370.6	1, 8700	< 0.0001
39	Age + Sex + CDS-2	6.03	5.71	529.5	1, 8700	< 0.0001
			Baseline model: model 40			
40	Age + Sex + # of Meds + Index-year Expenditures	32.90	--	--	--	--
41	Age + Sex + # of Meds + Index-year Expenditures + CCI-1	34.06	1.16	154.3	1, 8698	< 0.0001
42	Age + Sex + # of Meds + Index-year Expenditures + CCI-2	33.74	0.84	110.8	1, 8698	< 0.0001
43	Age + Sex + # of Meds + Index-year Expenditures + CDS-1	32.94	0.04	5.7	1, 8698	0.017
44	Age + Sex + # of Meds + Index-year Expenditures + CDS-2	32.95	0.05	7.5	1, 8698	0.063
			Baseline model: model 41			
45	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-1	34.06	0.00	0.5	1, 8697	0.46
46	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-2	34.06	0.00	1.0	1, 8697	0.31
			Baseline model: model 42			
47	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-1	33.73	-0.01	0.3	1, 8697	0.59
48	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-2	33.75	0.01	2.5	1, 8697	0.11

# of Meds: number of distinct medications; Adj. R^2: adjusted R^2 ; ΔR^2 : difference in R^2 ; d.f.: degrees of freedom

CCI-1 is based on Deyo RA, et al. "Adapting a Clinical Comorbidity Index for Use with ICD-9-CM Administrative Databases." *Journal of Clinical Epidemiology* 45, (1992): 613-19.

CCI-2 is based on Charlson ME, et al. "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients." *Journal of Clinical Epidemiology* 61, no. 12 (2008): 1234-40.

CDS-1 is based on Von Korff M, et al. "A Chronic Disease Score from Automated Pharmacy Data." *Journal of Clinical Epidemiology* 45, no. 2 (1992): 197-203.

CDS-2 is based on Clark DO, et al. "A Chronic Disease Score with Empirically Derived Weights." *Medical Care* 33, no. 8 (1995): 783-95.

3.2.4 Two-year High Healthcare Expenditures – Logistic Regression Models:

In predicting two-year high (≥ 90th percentile) healthcare expenditures, the index-year healthcare expenditures had the highest predictive power (*c* = .823), followed by the number of distinct medications (*c* = .771), CCI-2 (*c* = .754), CDS-2 (*c* = .744), CCI-1 (*c* = .737), and CDS-1 (*c* = .720), where age and sex were included in the models. Results from the Hosmer-Lemeshow goodness-of-fit tests indicated good model fit only for the model that included the number of distinct medications (χ^2 = 4.0; df = 8; p = .85), but poor model fits for the models that included the index-year total healthcare expenditures (χ^2 = 166.6; df = 8; p < .0001), CCI-1 (χ^2 = 19.3; df = 8; p = .013), CCI-2 (χ^2 = 16.7; df = 8; p = .033), CDS-1 (χ^2 = 30.0; df = 8; p = .0002), and CDS-2 (χ^2 = 76.5; df = 8; p < .0001).

With the inclusion of age, sex, number of distinct medications, and index-year total healthcare expenditures in the models, adding the CCI-1 or CCI-2 produced the same predictive power (*c* = .823). With the inclusion of age, sex, number of distinct medications, and index-year total healthcare expenditures in the models, adding the CDS-1 or CDS-2 produced similar predictive power (*c* = .817 for CDS-1; *c* = .820 for CDS-2). Results from the Hosmer-Lemeshow goodness-of-fit tests indicated poor model fit for all four models: the χ^2 was 17.6 for CCI-1 (df = 8; p = .024), 13.7 for CCI-2 (df = 8; p = .090), 19.4 for CDS-1 (df = 8; p = .013), and 24.6 for CDS-2 (df = 8; p = .0018).

The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-1, and CDS-1 produced a *c* statistic of .823, with good

model fit (χ^2 = 13.0; df = 8; p = .11). The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-1, and CDS-2 produced a *c* statistic of .824, with poor model fit (χ^2 = 16.1; df = 8; p = .041).

The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-2, and CDS-1 produced a *c* statistic of .823, with good model fit (χ^2 = 12.1; df = 8; p = .15). The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-2, and CDS-2 produced a *c* statistic of .824, with good model fit (χ^2 = 13.1; df = 8; p = .11).

Table 3.2.4 summarizes the results from section 3.2.4.

Table 3.2.4: Logistic Regression Modeling Results: Prediction of High (≥ 90th Percentile) Healthcare Expenditures in the Two-Year Post-Index Period

Models			Hosmer-Lemeshow Tests		
No.	Predictors	*c* statistic	χ^2	d.f.	*p* value
49	Age + Sex	0.575	7.5	8	0.49
50	Age + Sex + # of Meds	0.771	4.0		0.85
51	Age + Sex + Index-year Expenditures	0.823	166.6		< 0.0001
52	Age + Sex + CCI-1	0.737	19.3		0.013
53	Age + Sex + CCI-2	0.754	16.7		0.033
54	Age + Sex + CDS-1	0.720	30.0		0.0002
55	Age + Sex + CDS-2	0.744	76.5		< 0.0001
56	Age + Sex + # of Meds + Index-year Expenditures	0.818	27.3		0.0006
57	Age + Sex + # of Meds + Index-year Expenditures + CCI-1	0.823	17.6		0.024
58	Age + Sex + # of Meds + Index-year Expenditures + CCI-2	0.823	13.7		0.090
59	Age + Sex + # of Meds + Index-year Expenditures + CDS-1	0.817	19.4		0.013
60	Age + Sex + # of Meds + Index-year Expenditures + CDS-2	0.820	24.6		0.018
61	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-1	0.823	13.0		0.11
62	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-2	0.824	16.1		0.041
63	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-1	0.823	12.1		0.15
64	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-2	0.824	13.1		0.11

# of Meds: number of distinct medications; d.f.: degrees of freedom

CCI-1 is based on Deyo RA, et al. "Adapting a Clinical Comorbidity Index for Use with ICD-9-CM Administrative Databases." *Journal of Clinical Epidemiology* 45, (1992): 613-19.

CCI-2 is based on Charlson ME, et al. "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients." *Journal of Clinical Epidemiology* 61, no. 12 (2008): 1234-40.

CDS-1 is based on Von Korff M, et al. "A Chronic Disease Score from Automated Pharmacy Data." *Journal of Clinical Epidemiology* 45, no. 2 (1992): 197-203.

CDS-2 is based on Clark DO, et al. "A Chronic Disease Score with Empirically Derived Weights." *Medical Care* 33, no. 8 (1995): 783-95.

3.3 Modeling Results: Prediction of Number and Risk of Hospitalizations

3.3.1 One-year Number of Hospitalizations – Linear Regression Models:

Controlling for age and sex, all six predictors produced significant increases of variance explained in one-year number of hospitalizations: the number of distinct medications added an additional 6.0% of the variance ($F = 553.0$; $df = 1, 8700$; $p < .0001$); the index-year total healthcare expenditures added an additional 6.5% of the variance ($F = 605.5$; $df = 1, 8700$; $p < .0001$); CCI-1 added an additional 6.6% of the variance ($F = 619.2$; $df = 1, 8700$; $p < .0001$); CCI-2 added an additional 7.8% of the variance ($F = 739.3$; $df = 1, 8700$; $p < .0001$); CDS-1 added an additional 2.8% of the variance ($F = 254.5$; $df = 1, 8700$; $p < .0001$); and CDS-2 added an additional 3.5% of the variance ($F = 314.3$; $df = 1, 8700$; $p < .0001$).

Controlling for age, sex, number of distinct medications, and index-year total healthcare expenditures, adding the CCI-1 increased the variance explained by 1.6% ($F = 156.8$; $df = 1, 8698$; $p < .0001$), while adding the CCI-2 increased the variance explained by 1.8% ($F = 176.8$; $df = 1, 8698$; $p < .0001$). Including the CDS-1 in the model decreased the variance explained ($\Delta R^2 = -0.01\%$; $F = .8$; $df = 1, 8698$; $p = .38$), and including the CDS-2 increased the variance explained marginally ($\Delta R^2 = 0.01\%$; $F = 2.2$; $df = 1, 8698$; $p = .14$); however, neither results was significant statistically.

Controlling for age, sex, number of distinct medications, index-year total healthcare expenditures, and CCI-1, neither CDS-1 ($\Delta R^2 = 0.0\%$; $F = .7$; $df = 1, 8697$; $p =$

.42) nor CDS-2 (ΔR^2 = -0.01%; F = .1; df = 1, 8697; p = .80) explained a significant portion of the variance in one-year number of hospitalizations.

Controlling for age, sex, number of distinct medications, index-year total healthcare expenditures, and CCI-2, neither CDS-1 (ΔR^2 = 0.02%; F = 2.2; df = 1, 8697; p = .14) nor CDS-2 (ΔR^2 = -0.01%; F = 0; df = 1, 8697; p = .97) explained a significant portion of the variance in one-year number of hospitalizations.

Table 3.3.1 summarizes results from section 3.3.1.

Table 3.3.1: Linear Regression Modeling Results: Prediction of Number of Hospitalizations in the One-Year Post-Index Period

Models			**R^2 Difference Tests**			
No.	Predictors	Adj. R^2 (%)	ΔR^2 (%)	F value	d.f.	*p* value
			Baseline model: model 66			
65	Age + Sex	0.25	--	--	--	--
66	Age + Sex + # of Meds	6.20	5.95	553.0	1, 8700	< 0.0001
67	Age + Sex + Index-year Expenditures	6.74	6.49	605.5	1, 8700	< 0.0001
68	Age + Sex + CCI-1	6.87	6.62	619.2	1, 8700	< 0.0001
69	Age + Sex + CCI-2	8.05	7.80	739.3	1, 8700	< 0.0001
70	Age + Sex + CDS-1	3.07	2.82	254.5	1, 8700	< 0.0001
71	Age + Sex + CDS-2	3.72	3.47	314.3	1, 8700	< 0.0001
			Baseline model: model 72			
72	Age + Sex + # of Meds + Index-year Expenditures	9.76	--	--	--	--
73	Age + Sex + # of Meds + Index-year Expenditures + CCI-1	11.34	1.58	156.8	1, 8698	< 0.0001
74	Age + Sex + # of Meds + Index-year Expenditures + CCI-2	11.54	1.78	176.8	1, 8698	< 0.0001
75	Age + Sex + # of Meds + Index-year Expenditures + CDS-1	9.75	-0.01	0.8	1, 8698	0.38
76	Age + Sex + # of Meds + Index-year Expenditures + CDS-2	9.77	0.01	2.2	1, 8698	0.14
			Baseline model: model 73			
77	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-1	11.34	0.00	0.7	1, 8697	0.42
78	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-2	11.33	-0.01	0.1	1, 8697	0.80
			Baseline model: model 74			
79	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-1	11.56	0.02	2.2	1, 8697	0.14
80	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-2	11.53	-0.01	0.0	1, 8697	0.97

# of Meds: number of distinct medications; Adj. R^2: adjusted R^2 ; ΔR^2 : difference in R^2 ; d.f.: degrees of freedom

CCI-1 is based on Deyo RA, et al. "Adapting a Clinical Comorbidity Index for Use with ICD-9-CM Administrative Databases." *Journal of Clinical Epidemiology* 45, (1992): 613-19.

CCI-2 is based on Charlson ME, et al. "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients." *Journal of Clinical Epidemiology* 61, no. 12 (2008): 1234-40.

CDS-1 is based on Von Korff M, et al. "A Chronic Disease Score from Automated Pharmacy Data." *Journal of Clinical Epidemiology* 45, no. 2 (1992): 197-203.

CDS-2 is based on Clark DO, et al. "A Chronic Disease Score with Empirically Derived Weights." *Medical Care* 33, no. 8 (1995): 783-95.

3.3.2 One-year Risk of Hospitalization – Logistic Regression Models:

In predicting one-year risk of hospitalization, the index-year healthcare expenditures had the highest predictive power (*c* = .684), followed by the number of distinct medications (*c* = .677), CCI-2 (*c* = .658), CDS-2 (*c* = .649), CCI-1 (*c* = .645), and CDS-1 (*c* = .635), where age and sex were included in the models. Results from the Hosmer-Lemeshow goodness-of-fit tests indicated good model fit for the models that included the number of distinct medications (χ^2 = 9.1; df = 8; p = .34) and CCI-1 (χ^2 = 10.6; df = 8; p = .22), but poor model fits for the models that included the index-year total healthcare expenditures (χ^2 = 118.4; df = 8; p < .0001), CCI-2 (χ^2 = 16.7; df = 8; p = .033), CDS-1 (χ^2 = 16.2; df = 8; p = .040), and CDS-2 (χ^2 = 42.3; df = 8; p < .0001).

With the inclusion of age, sex, number of distinct medications, and index-year total healthcare expenditures in the models, both CCI-1 and CCI-2 had the same predictive power (*c* = .701), and both CDS-1 and CDS-2 had the same predictive power (*c* = .692). Results from the Hosmer-Lemeshow goodness-of-fit tests indicated good model fit for all four models: the χ^2 was 7.6 for CCI-1 (df = 8; p = .47), 8.2 for CCI-2 (df = 8; p = .41), 9.7 for CDS-1 (df = 8; p = .29), and 8.6 for CDS-2 (df = 8; p = .37).

The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-1, and CDS-1 produced a *c* statistic of .700, with good model fit (χ^2 = 10.4; df = 8; p = .24). The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-1, and CDS-2 produced a *c* statistic of .701, with good model fit (χ^2 = 6.2; df = 8; p = .62).

The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-2, and CDS-1 produced a *c* statistic of .701, with good model fit ($\chi^2 = 7.2$; df = 8; p = .52). The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-2, and CDS-2 also produced a *c* statistic of .701, with good model fit ($\chi^2 = 10.1$; df = 8; p = .26).

Table 3.3.2 summarizes the results from section 3.3.2.

Table 3.3.2: Logistic Regression Modeling Results: Prediction of Risk (≥ 1 Admission) of Hospitalizations in the One-Year Post-Index Period

Models			**Hosmer-Lemeshow Tests**		
No.	Predictors	*c* statistic	χ^2	d.f.	*p* value
81	Age + Sex	0.545	30.3	8	0.0002
82	Age + Sex + # of Meds	0.677	9.1		0.34
83	Age + Sex + Index-year Expenditures	0.684	118.4		< 0.0001
84	Age + Sex + CCI-1	0.645	10.6		0.22
85	Age + Sex + CCI-2	0.658	16.7		0.033
86	Age + Sex + CDS-1	0.635	16.2		0.040
87	Age + Sex + CDS-2	0.649	42.3		< 0.0001
88	Age + Sex + # of Meds + Index-year Expenditures	0.692	11.4		0.18
89	Age + Sex + # of Meds + Index-year Expenditures + CCI-1	0.701	7.6		0.47
90	Age + Sex + # of Meds + Index-year Expenditures + CCI-2	0.701	8.2		0.41
91	Age + Sex + # of Meds + Index-year Expenditures + CDS-1	0.692	9.7		0.29
92	Age + Sex + # of Meds + Index-year Expenditures + CDS-2	0.692	8.6		0.37
93	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-1	0.700	10.4		0.24
94	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-2	0.701	6.2		0.62
95	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-1	0.701	7.2		0.52
96	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-2	0.701	10.1		0.26

# of Meds: number of distinct medications; d.f.: degrees of freedom

CCI-1 is based on Deyo RA, et al. "Adapting a Clinical Comorbidity Index for Use with ICD-9-CM Administrative Databases." *Journal of Clinical Epidemiology* 45, (1992): 613-19.

CCI-2 is based on Charlson ME, et al. "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients." *Journal of Clinical Epidemiology* 61, no. 12 (2008): 1234-40.

CDS-1 is based on Von Korff M, et al. "A Chronic Disease Score from Automated Pharmacy Data." *Journal of Clinical Epidemiology* 45, no. 2 (1992): 197-203.

CDS-2 is based on Clark DO, et al. "A Chronic Disease Score with Empirically Derived Weights." *Medical Care* 33, no. 8 (1995): 783-95.

3.3.3 Two-year Number of Hospitalizations – Linear Regression Models:

Controlling for age and sex, all six predictors produced significant increases of variance explained in two-year number of hospitalizations: the number of distinct medications added an additional 7.4% of the variance ($F = 693.0$; $df = 1, 8700$; $p < .0001$); the index-year total healthcare expenditures added an additional 7.0% of the variance ($F = 656.1$; $df = 1, 8700$; $p < .0001$); CCI-1 added an additional 7.8% of the variance ($F = 736.5$; $df = 1, 8700$; $p < .0001$); CCI-2 added an additional 9.0% of the variance ($F = 860.5$; $df = 1, 8700$; $p < .0001$); CDS-1 added an additional 3.4% of the variance ($F = 303.6$; $df = 1, 8700$; $p < .0001$); and CDS-2 added an additional 4.6% of the variance ($F = 419.5$; $df = 1, 8700$; $p < .0001$).

Controlling for age, sex, number of distinct medications, and index-year total healthcare expenditures, adding the CCI-1 increased the variance explained by 1.9% ($F = 192.4$; $df = 1, 8698$; $p < .0001$), adding the CCI-2 increased the variance explained by 2.0% ($F = 203.1$; $df = 1, 8698$; $p < .0001$), and adding the CDS-2 increased the variance explained by 0.07% ($F = 7.8$; $df = 1, 8698$; $p = .0054$); however, adding the CDS-1 decreased the variance explained by 0.01% ($F = .3$; $df = 1, 8698$; $p = .62$).

Controlling for age, sex, number of distinct medications, index-year total healthcare expenditures, and CCI-1, neither CDS-1 ($\Delta R^2 = 0.01\%$; $F = 1.9$; $df = 1, 8697$; $p = .17$) nor CDS-2 ($\Delta R^2 = 0.0\%$; $F = .8$; $df = 1, 8697$; $p = .38$) explained a significant portion of the variance in two-year number of hospitalizations.

Controlling for age, sex, number of distinct medications, index-year total healthcare expenditures, and CCI-2, CDS-1 explained a significant portion of the variance in two-year number of hospitalizations (ΔR^2 = 0.04%; F = 4.2; df = 1, 8697; p = .040), but CDS-2 did not (ΔR^2 = 0.0%; F = 1.5; df = 1, 8697; p = .21)

Table 3.3.3 summarizes the results from section 3.3.3.

Table 3.3.3: Linear Regression Modeling Results: Prediction of Number of Hospitalizations in the Two-Year Post-Index Period

Models			**R^2 Difference Tests**			
No.	Predictors	Adj. R^2 (%)	ΔR^2 (%)	F value	d.f.	*p* value
			Baseline model: model 97			
97	Age + Sex	0.29	--	--	--	--
98	Age + Sex + # of Meds	7.64	7.35	693.0	1, 8700	< 0.0001
99	Age + Sex + Index-year Expenditures	7.28	6.99	656.1	1, 8700	< 0.0001
100	Age + Sex + CCI-1	8.06	7.77	736.5	1, 8700	< 0.0001
101	Age + Sex + CCI-2	9.26	8.97	860.5	1, 8700	< 0.0001
102	Age + Sex + CDS-1	3.64	3.35	303.6	1, 8700	< 0.0001
103	Age + Sex + CDS-2	4.87	4.58	419.5	1, 8700	< 0.0001
			Baseline model: model 104			
104	Age + Sex + # of Meds + Index-year Expenditures	11.25	--	--	--	--
105	Age + Sex + # of Meds + Index-year Expenditures + CCI-1	13.16	1.91	192.4	1, 8698	< 0.0001
106	Age + Sex + # of Meds + Index-year Expenditures + CCI-2	13.26	2.01	203.1	1, 8698	< 0.0001
107	Age + Sex + # of Meds + Index-year Expenditures + CDS-1	11.24	-0.01	0.3	1, 8698	0.62
108	Age + Sex + # of Meds + Index-year Expenditures + CDS-2	11.32	0.07	7.8	1, 8698	0.0054
			Baseline model: model 105			
109	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-1	13.17	0.01	1.9	1, 8697	0.17
110	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-2	13.16	0.00	0.8	1, 8697	0.38
			Baseline model: model 106			
111	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-1	13.30	0.04	4.2	1, 8697	0.040
112	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-2	13.27	0.01	1.5	1, 8697	0.21

# of Meds: number of distinct medications; Adj. R^2: adjusted R^2 ; ΔR^2 : difference in R^2 ; d.f.: degrees of freedom

CCI-1 is based on Deyo RA, et al. "Adapting a Clinical Comorbidity Index for Use with ICD-9-CM Administrative Databases." *Journal of Clinical Epidemiology* 45, (1992): 613-19.

CCI-2 is based on Charlson ME, et al. "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients." *Journal of Clinical Epidemiology* 61, no. 12 (2008): 1234-40.

CDS-1 is based on Von Korff M, et al. "A Chronic Disease Score from Automated Pharmacy Data." *Journal of Clinical Epidemiology* 45, no. 2 (1992): 197-203.

CDS-2 is based on Clark DO, et al. "A Chronic Disease Score with Empirically Derived Weights." *Medical Care* 33, no. 8 (1995): 783-95.

3.3.4 Two-year Risk of Hospitalization – Logistic Regression Models:

In predicting two-year risk of hospitalization, the index-year healthcare expenditures had the highest predictive power (*c* = .676), followed by the number of distinct medications (*c* = .663), CCI-2 (*c* = .642), CDS-2 (*c* = .638), CCI-1 (*c* = .631), and CDS-1 (*c* = .619), where age and sex were included in the models. Results from the Hosmer-Lemeshow goodness-of-fit tests indicated good model fit for the model that included the number of distinct medications (χ^2 = 12.2; df = 8; p = .14), but poor model fits for the models that included the index-year total healthcare expenditures (χ^2 = 136.2; df = 8; p < .0001), CCI-1 (χ^2 = 21.3; df = 8; p = .0065), CCI-2 (χ^2 = 20.2; df = 8; p = .0095), CDS-1 (χ^2 = 19.1; df = 8; p = .014), and CDS-2 (χ^2 = 59.5; df = 8; p < .0001).

With the inclusion of age, sex, number of distinct medications, and index-year total healthcare expenditures in the models, the CCI-1 (*c* = .689) and CCI-2 (*c* = .688) had similar predictive power, and the CDS-1 and CDS-2 had similar predictive power (*c* = .681 for CDS-1; *c* = .682 for CDS-2). Results from the Hosmer-Lemeshow goodness-of-fit tests indicated good model fit for the model including CCI-2 (χ^2 = 11.2; df = 8; p = .19) but poor model fit for the models that included CCI-1 (χ^2 = 16.9; df = 8; p = .031), CDS-1 (χ^2 = 18.4; df = 8; p = .019), and CDS-2 (χ^2 = 17.0; df = 8; p = .030).

The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-1, and CDS-1 produced a *c* statistic of .689, with poor model fit (χ^2 = 17.4; df = 8; p = .026). The model that included age, sex, number of

distinct medications, index-year healthcare expenditures, CCI-1, and CDS-2 also produced a *c* statistic of .689, with poor model fit ($\chi^2 = 15.6$; df = 8; p = .049).

The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-2, and CDS-1 produced a *c* statistic of .688, with good model fit ($\chi^2 = 11.9$; df = 8; p = .16). The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-2, and CDS-2 also produced a *c* statistic of .688, with good model fit ($\chi^2 = 11.4$; df = 8; p = .18).

Table 3.3.4 summarizes the results from section 3.3.4.

Table 3.3.4: Logistic Regression Modeling Results: Prediction of Risk (≥ 1 Admission) of Hospitalizations in the Two-Year Post-Index Period

Models			**Hosmer-Lemeshow Tests**		
No.	Predictors	*c* statistic	χ^2	d.f.	*p* value
113	Age + Sex	0.538	54.9	8	< 0.0001
114	Age + Sex + # of Meds	0.663	12.2		0.14
115	Age + Sex + Index-year Expenditures	0.676	136.2		< 0.0001
116	Age + Sex + CCI-1	0.631	21.3		0.0065
117	Age + Sex + CCI-2	0.642	20.2		0.0095
118	Age + Sex + CDS-1	0.619	19.1		0.014
119	Age + Sex + CDS-2	0.638	59.5		< 0.0001
120	Age + Sex + # of Meds + Index-year Expenditures	0.681	18.1		0.020
121	Age + Sex + # of Meds + Index-year Expenditures + CCI-1	0.689	16.9		0.031
122	Age + Sex + # of Meds + Index-year Expenditures + CCI-2	0.688	11.2		0.19
123	Age + Sex + # of Meds + Index-year Expenditures + CDS-1	0.681	18.4		0.019
124	Age + Sex + # of Meds + Index-year Expenditures + CDS-2	0.682	17.0		0.030
125	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-1	0.689	17.4		0.026
126	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-2	0.689	15.6		0.049
127	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-1	0.688	11.9		0.16
128	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-2	0.688	11.4		0.18

# of Meds: number of distinct medications; d.f.: degrees of freedom

CCI-1 is based on Deyo RA, et al. "Adapting a Clinical Comorbidity Index for Use with ICD-9-CM Administrative Databases." *Journal of Clinical Epidemiology* 45, (1992): 613-19.

CCI-2 is based on Charlson ME, et al. "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients." *Journal of Clinical Epidemiology* 61, no. 12 (2008): 1234-40.

CDS-1 is based on Von Korff M, et al. "A Chronic Disease Score from Automated Pharmacy Data." *Journal of Clinical Epidemiology* 45, no. 2 (1992): 197-203.

CDS-2 is based on Clark DO, et al. "A Chronic Disease Score with Empirically Derived Weights." *Medical Care* 33, no. 8 (1995): 783-95.

3.4 Modeling Results: Prediction of Number and Risk of Emergency Department Visits

3.4.1 One-year number of emergency department visits – linear regression models:

Controlling for age and sex, all six predictors produced significant increases of variance explained in one-year number of emergency department visits: the number of distinct medications added an additional 8.5% of the variance ($F = 825.2$; $df = 1, 8700$; $p < .0001$); the index-year total healthcare expenditures added an additional 4.8% of the variance ($F = 446.7$; $df = 1, 8700$; $p < .0001$); CCI-1 added an additional 4.5% of the variance ($F = 420.6$; $df = 1, 8700$; $p < .0001$); CCI-2 added an additional 5.8% of the variance ($F = 546.9$; $df = 1, 8700$; $p < .0001$); CDS-1 added an additional 3.2% of the variance ($F = 290.5$; $df = 1, 8700$; $p < .0001$); and CDS-2 added an additional 5.2% of the variance ($F = 486.6$; $df = 1, 8700$; $p < .0001$).

Controlling for age, sex, number of distinct medications, and index-year total healthcare expenditures, adding the CCI-1 increased the variance explained by 0.5% ($F = 51.2$; $df = 1, 8698$; $p < .0001$), while adding the CCI-2 increased the variance explained by 0.6% ($F = 61.5$; $df = 1, 8698$; $p < .0001$); adding the CDS-1 increased the variance explained by 0.03% ($F = 4.1$; $df = 1, 8698$; $p = .042$) and adding the CDS-2 increased the variance explained by 0.1% ($F = 11.0$; $df = 1, 8698$; $p = .0009$).

Controlling for age, sex, number of distinct medications, index-year total healthcare expenditures, and CCI-1, both CDS-1 ($\Delta R^2 = 0.08\%$; $F = 9.2$; $df = 1, 8697$; $p = .0024$) and CDS-2 ($\Delta R^2 = 0.05\%$; $F = 5.5$; $df = 1, 8697$; $p = .019$) explained significant portions of the variance in one-year number of emergency department visits.

Controlling for age, sex, number of distinct medications, index-year total healthcare expenditures, and CCI-2, both CDS-1 (ΔR^2 = 0.11%; F = 12.1; df = 1, 8697; p = .0005) and CDS-2 (ΔR^2 = 0.10%; F = 6.1; df = 1, 8697; p = .013) explained significant portions of the variance in one-year number of emergency department visits.

Table 3.4.1 summarizes the results from section 3.4.1.

Table 3.4.1: Linear Regression Modeling Results: Prediction of Number of Emergency Department Visits in the One-Year Post-Index Period

Models			**R^2 Difference Tests**			
No.	Predictors	Adj. R^2 (%)	ΔR^2 (%)	F value	d.f.	*p* value
			Baseline model: model 129			
129	Age + Sex	1.35	--	--	--	--
130	Age + Sex + # of Meds	9.89	8.54	825.2	1, 8700	< 0.0001
131	Age + Sex + Index-year Expenditures	6.16	4.81	446.7	1, 8700	< 0.0001
132	Age + Sex + CCI-1	5.89	4.54	420.6	1, 8700	< 0.0001
133	Age + Sex + CCI-2	7.18	5.83	546.9	1, 8700	< 0.0001
134	Age + Sex + CDS-1	4.53	3.18	290.5	1, 8700	< 0.0001
135	Age + Sex + CDS-2	6.57	5.22	486.6	1, 8700	< 0.0001
			Baseline model: model 136			
136	Age + Sex + # of Meds + Index-year Expenditures	11.74	--	--	--	--
137	Age + Sex + # of Meds + Index-year Expenditures + CCI-1	12.24	0.50	51.2	1, 8698	< 0.0001
138	Age + Sex + # of Meds + Index-year Expenditures + CCI-2	12.35	0.61	61.5	1, 8698	< 0.0001
139	Age + Sex + # of Meds + Index-year Expenditures + CDS-1	11.77	0.03	4.1	1, 8698	0.042
140	Age + Sex + # of Meds + Index-year Expenditures + CDS-2	11.84	0.10	11.0	1, 8698	0.0009
			Baseline model: model 137			
141	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-1	12.32	0.08	9.2	1, 8697	0.0024
142	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-2	12.29	0.05	5.5	1, 8697	0.019
			Baseline model: model 138			
143	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-1	12.46	0.11	12.1	1, 8697	0.0005
144	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-2	12.45	0.10	6.1	1, 8697	0.013

# of Meds: number of distinct medications; Adj. R^2: adjusted R^2 ; ΔR^2 : difference in R^2 ; d.f.: degrees of freedom

CCI-1 is based on Deyo RA, et al. "Adapting a Clinical Comorbidity Index for Use with ICD-9-CM Administrative Databases." *Journal of Clinical Epidemiology* 45, (1992): 613-19.

CCI-2 is based on Charlson ME, et al. "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients." *Journal of Clinical Epidemiology* 61, no. 12 (2008): 1234-40.

CDS-1 is based on Von Korff M, et al. "A Chronic Disease Score from Automated Pharmacy Data." *Journal of Clinical Epidemiology* 45, no. 2 (1992): 197-203.

CDS-2 is based on Clark DO, et al. "A Chronic Disease Score with Empirically Derived Weights." *Medical Care* 33, no. 8 (1995): 783-95.

3.4.2 One-year Risk of Emergency Department Visit – Logistic Regression Models:

In predicting one-year risk of emergency department visit, the number of distinct medications had the highest predictive power (*c* = .653), followed by CDS-2 (*c* = .624), CCI-2 (*c* = .621), CDS-1 (*c* = .619), index-year healthcare expenditures (*c* = .617), and CCI-1 (*c* = .614), where age and sex were included in the models. Results from the Hosmer-Lemeshow goodness-of-fit tests indicated good model fit for the models that included the number of distinct medications (χ^2 = 7.2; df = 8; p = .51), CCI-1 (χ^2 = 3.5; df = 8; p = .90), CCI-2 (χ^2 = 6.1; df = 8; p = .64), CDS-1 (χ^2 = 5.2; df = 8; p = .74), and CDS-2 (χ^2 = 15.1; df = 8; p = .057), but poor model fit for the model that included the index-year total healthcare expenditures (χ^2 = 39.7; df = 8; p = < .0001).

With the inclusion of age, sex, number of distinct medications, and index-year total healthcare expenditures in the models, the CCI-1 produced a *c* statistic of .659 and the CCI-2 produced a *c* statistic of .660; the CDS-1 and CDS-2 both produced a *c* statistic of .656. Results from the Hosmer-Lemeshow goodness-of-fit tests indicated good model fit for all four models: the χ^2 was 13.6 for CCI-1 (df = 8; p = .092), 10.9 for CCI-2 (df = 8; p = .21), 6.7 for CDS-1 (df = 8; p = .56), and 9.4 for CDS-2 (df = 8; p = .31).

The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-1, and CDS-1 produced a *c* statistic of .659, with good model fit (χ^2 = 12.3; df = 8; p = .14). The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-1, and CDS-2 produced a *c* statistic of .660, with good model fit (χ^2 = 11.2; df = 8; p = .19).

The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-2, and CDS-1 produced a *c* statistic of .660, with good model fit ($\chi^2 = 11.3$; df = 8; p = .18). The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-2, and CDS-2 also produced a *c* statistic of .660, with good model fit ($\chi^2 = 9.4$; df = 8; p = .31).

Table 3.4.2 summarizes the results from section 3.4.2.

Table 3.4.2: Logistic Regression Modeling Results: Prediction of Risk (≥ 1 Visit) of Emergency Department Visits in the One-Year Post-Index Period

Models			**Hosmer-Lemeshow Tests**		
No.	Predictors	*c* statistic	χ^2	d.f.	*p* value
145	Age + Sex	0.563	10.3	8	0.24
146	Age + Sex + # of Meds	0.653	7.2		0.51
147	Age + Sex + Index-year Expenditures	0.617	39.7		< 0.0001
148	Age + Sex + CCI-1	0.614	3.5		0.90
149	Age + Sex + CCI-2	0.621	6.1		0.64
150	Age + Sex + CDS-1	0.619	5.2		0.74
151	Age + Sex + CDS-2	0.624	15.1		0.057
152	Age + Sex + # of Meds + Index-year Expenditures	0.656	7.0		0.54
153	Age + Sex + # of Meds + Index-year Expenditures + CCI-1	0.659	13.6		0.092
154	Age + Sex + # of Meds + Index-year Expenditures + CCI-2	0.660	10.9		0.21
155	Age + Sex + # of Meds + Index-year Expenditures + CDS-1	0.656	6.7		0.56
156	Age + Sex + # of Meds + Index-year Expenditures + CDS-2	0.656	9.4		0.31
157	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-1	0.659	12.3		0.14
158	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-2	0.660	11.2		0.19
159	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-1	0.660	11.3		0.18
160	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-2	0.660	9.4		0.31

# of Meds: number of distinct medications; d.f.: degrees of freedom

CCI-1 is based on Deyo RA, et al. "Adapting a Clinical Comorbidity Index for Use with ICD-9-CM Administrative Databases." *Journal of Clinical Epidemiology* 45, (1992): 613-19.

CCI-2 is based on Charlson ME, et al. "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients." *Journal of Clinical Epidemiology* 61, no. 12 (2008): 1234-40.

CDS-1 is based on Von Korff M, et al. "A Chronic Disease Score from Automated Pharmacy Data." *Journal of Clinical Epidemiology* 45, no. 2 (1992): 197-203.

CDS-2 is based on Clark DO, et al. "A Chronic Disease Score with Empirically Derived Weights." *Medical Care* 33, no. 8 (1995): 783-95.

3.4.3 Two-year Number of Emergency Department Visits – Linear Regression Models:

Controlling for age and sex, all six predictors produced significant increases of variance explained in two-year number of emergency department visits: the number of distinct medications added an additional 10.3% of the variance ($F = 1024.5$; $df = 1, 8700$; $p < .0001$); the index-year total healthcare expenditures added an additional 5.2% of the variance ($F = 487.2$; $df = 1, 8700$; $p < .0001$); CCI-1 added an additional 5.4% of the variance ($F = 504.1$; $df = 1, 8700$; $p < .0001$); CCI-2 added an additional 6.7% of the variance ($F = 639.6$; $df = 1, 8700$; $p < .0001$); CDS-1 added an additional 4.0% of the variance ($F = 373.6$; $df = 1, 8700$; $p < .0001$); and CDS-2 added an additional 6.5% of the variance ($F = 616.8$; $df = 1, 8700$; $p < .0001$).

Controlling for age, sex, number of distinct medications, and index-year total healthcare expenditures, adding the CCI-1 increased the variance explained by 0.6% ($F = 65.8$; $df = 1, 8698$; $p < .0001$), and adding the CCI-2 increased the variance explained by 0.7% ($F = 71.1$; $df = 1, 8698$; $p < .0001$), and adding the CDS-2 increased the variance explained by 0.2% ($F = 18.5$; $df = 1, 8698$; $p = < .0001$); however, inclusion of the CDS-1 did not increase the variance explained significantly ($\Delta R^2 = 0.02\%$; $F = 2.7$; $df = 1, 8698$; $p = .10$).

Controlling for age, sex, number of distinct medications, index-year total healthcare expenditures, and CCI-1, both CDS-1 ($\Delta R^2 = 0.07\%$; $F = 7.7$; $df = 1, 8697$; $p = .0056$) and CDS-2 ($\Delta R^2 = 0.09\%$; $F = 10.3$; $df = 1, 8697$; $p = .0014$) explained significant portions of the variance in two-year number of emergency department visits.

Controlling for age, sex, number of distinct medications, index-year total healthcare expenditures, and CCI-2, both CDS-1 (ΔR^2 = 0.1%; F = 10.2; df = 1, 8697; p = .0014) and CDS-2 (ΔR^2 = 0.1%; F = 11.6; df = 1, 8697; p = .0007) explained significant portions of the variance in two-year number of emergency department visits.

Table 3.4.3 summarizes the results from section 3.4.3.

Table 3.4.3: Linear Regression Modeling Results: Prediction of Number of Emergency Department Visits in the Two-Year Post-Index Period

Models			**R^2 Difference Tests**			
No.	Predictors	Adj. R^2 (%)	ΔR^2 (%)	F value	d.f.	*p* value
			Baseline model: model 161			
161	Age + Sex	2.14	--	--	--	--
162	Age + Sex + # of Meds	12.44	10.30	1024.5	1, 8700	< 0.0001
163	Age + Sex + Index-year Expenditures	7.32	5.18	487.2	1, 8700	< 0.0001
164	Age + Sex + CCI-1	7.49	5.35	504.1	1, 8700	< 0.0001
165	Age + Sex + CCI-2	8.83	6.69	639.6	1, 8700	< 0.0001
166	Age + Sex + CDS-1	6.16	4.02	373.6	1, 8700	< 0.0001
167	Age + Sex + CDS-2	8.61	6.47	616.8	1, 8700	< 0.0001
			Baseline model: model 168			
168	Age + Sex + # of Meds + Index-year Expenditures	14.27	--	--	--	--
169	Age + Sex + # of Meds + Index-year Expenditures + CCI-1	14.90	0.63	65.8	1, 8698	< 0.0001
170	Age + Sex + # of Meds + Index-year Expenditures + CCI-2	14.95	0.68	71.1	1, 8698	< 0.0001
171	Age + Sex + # of Meds + Index-year Expenditures + CDS-1	14.29	0.02	2.7	1, 8698	0.10
172	Age + Sex + # of Meds + Index-year Expenditures + CDS-2	14.44	0.17	18.5	1, 8698	< 0.0001
			Baseline model: model 169			
173	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-1	14.97	0.07	7.7	1, 8697	0.0056
174	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-2	14.99	0.09	10.3	1, 8697	0.014
			Baseline model: model 170			
175	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-1	15.04	0.09	10.2	1, 8697	0.0014
176	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-2	15.06	0.11	11.6	1, 8697	0.0007

# of Meds: number of distinct medications; Adj. R^2: adjusted R^2 ; ΔR^2 : difference in R^2 ; d.f.: degrees of freedom

CCI-1 is based on Deyo RA, et al. "Adapting a Clinical Comorbidity Index for Use with ICD-9-CM Administrative Databases." *Journal of Clinical Epidemiology* 45, (1992): 613-19.

CCI-2 is based on Charlson ME, et al. "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients." *Journal of Clinical Epidemiology* 61, no. 12 (2008): 1234-40.

CDS-1 is based on Von Korff M, et al. "A Chronic Disease Score from Automated Pharmacy Data." *Journal of Clinical Epidemiology* 45, no. 2 (1992): 197-203.

CDS-2 is based on Clark DO, et al. "A Chronic Disease Score with Empirically Derived Weights." *Medical Care* 33, no. 8 (1995): 783-95.

3.4.4 Two-year Risk of Emergency Department Visits – Logistic Regression Models:

In predicting two-year risk of emergency department visits, the number of distinct medications had the highest predictive power (*c* = .654), followed by CDS-2 (*c* = .626), index-year healthcare expenditures (*c* = .623), CCI-2 (*c* = .619), CDS-2 (*c* = .618), and CCI-1 (*c* = .611), where age and sex were included in the models. Results from the Hosmer-Lemeshow goodness-of-fit tests indicated good model fit for the models that included the number of distinct medications (χ^2 = 8.4; df = 8; p = .39), CCI-1 (χ^2 = 5.8; df = 8; p = .69), CCI-2 (χ^2 = 9.6; df = 8; p = .30), CDS-1 (χ^2 = 12.4; df = 8; p = .14), and CDS-2 (χ^2 = 8.2; df = 8; p = .42). The model that included the index-year total healthcare expenditures had poor model fit (χ^2 = 18.5; df = 8; p = .018).

With the inclusion of age, sex, number of distinct medications, and index-year total healthcare expenditures in the models, the CCI-1 and CCI-2 produced a *c* statistic of .660, while the CDS-1 and CDS-2 produced a *c* statistic of .657. Results from the Hosmer-Lemeshow goodness-of-fit tests indicated poor model fit for the model that included the CCI-1 (χ^2 = 15.7; df = 8; p = .047). The fit was good for the models that included the CCI-2 (χ^2 = 12.0; df = 8; p = .15), CDS-1 (χ^2 = 4.9; df = 8; p = .76), and CDS-2 (χ^2 = 4.8; df = 8; p = .78).

The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-1, and CDS-1 produced a *c* statistic of .660, with poor model fit (χ^2 = 16.1; df = 8; p = .041). The model that included age, sex, number of

distinct medications, index-year healthcare expenditures, CCI-1, and CDS-2 produced a *c* statistic of .660, with good model fit ($\chi^2 = 8.0$; df = 8; p = .43).

The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-2, and CDS-1 produced a *c* statistic of .660, with good model fit ($\chi^2 = 10.8$; df = 8; p = .21). The model that included age, sex, number of distinct medications, index-year healthcare expenditures, CCI-2, and CDS-2 also produced a *c* statistic of .660, with good model fit ($\chi^2 = 8.3$; df = 8; p = .41).

Table 3.4.4 summarizes the results from section 3.4.4.

Table 3.4.4: Logistic Regression Modeling Results: Prediction of Risk (≥ 1 Visit) of Emergency Department Visits in the Two-Year Post-Index Period

Models			**Hosmer-Lemeshow Tests**		
No.	Predictors	*c* statistic	χ^2	d.f.	*p* value
177	Age + Sex	0.566	25.3	8	0.0014
178	Age + Sex + # of Meds	0.654	8.4		0.39
179	Age + Sex + Index-year Expenditures	0.623	18.5		0.018
180	Age + Sex + CCI-1	0.611	5.8		0.69
181	Age + Sex + CCI-2	0.619	9.6		0.30
182	Age + Sex + CDS-1	0.618	12.4		0.14
183	Age + Sex + CDS-2	0.626	8.2		0.42
184	Age + Sex + # of Meds + Index-year Expenditures	0.657	3.6		0.89
185	Age + Sex + # of Meds + Index-year Expenditures + CCI-1	0.660	15.7		0.047
186	Age + Sex + # of Meds + Index-year Expenditures + CCI-2	0.660	12.0		0.15
187	Age + Sex + # of Meds + Index-year Expenditures + CDS-1	0.657	4.9		0.76
188	Age + Sex + # of Meds + Index-year Expenditures + CDS-2	0.657	4.8		0.78
189	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-1	0.660	16.1		0.041
190	Age + Sex + # of Meds + Index-year Expenditures + CCI-1 + CDS-2	0.660	8.0		0.43
191	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-1	0.660	10.8		0.21
192	Age + Sex + # of Meds + Index-year Expenditures + CCI-2 + CDS-2	0.660	8.3		0.41

# of Meds: number of distinct medications; d.f.: degrees of freedom

CCI-1 is based on Deyo RA, et al. "Adapting a Clinical Comorbidity Index for Use with ICD-9-CM Administrative Databases." *Journal of Clinical Epidemiology* 45, (1992): 613-19.

CCI-2 is based on Charlson ME, et al. "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients." *Journal of Clinical Epidemiology* 61, no. 12 (2008): 1234-40.

CDS-1 is based on Von Korff M, et al. "A Chronic Disease Score from Automated Pharmacy Data." *Journal of Clinical Epidemiology* 45, no. 2 (1992): 197-203.

CDS-2 is based on Clark DO, et al. "A Chronic Disease Score with Empirically Derived Weights." *Medical Care* 33, no. 8 (1995): 783-95.

Chapter 4 Discussion and Conclusions

4.1 Overview

The predicative validity of six comorbidity adjustment measures was compared using administrative claims data from the Department of Defense TRICARE insurance program for a group of diabetic patients. These measures included: 1) number of distinct medications, 2) index-year total healthcare expenditures, 3) CCI-1, 4) CCI-2, 5) CDS-1, and 6) CDS-2. In predicting total healthcare expenditures over one year and two years, the sum of index-year healthcare expenditures ($model_3$; $model_{35}$) was notably better than the other five measures. For the prediction of hospitalization over one year and two years, the CCI-2 performed the best in the linear regression models ($model_{69}$; $model_{101}$), and the sum of index-year healthcare expenditures was the best predictor in the logistic regression models ($model_{83}$; $model_{115}$). In predicting use of emergency department over one year and two years, the number of distinct medications performed the best ($model_{130}$; $model_{162}$). Overall, these measures appeared to be more robust predictors of future healthcare expenditures than hospitalizations or emergency department visits. Table 4.1 summarizes the top two performing comorbidity adjustment measures for the prediction of each outcome variable.

Table 4.1: Top Two Performing Comorbidity Adjustment Measures for the Prediction of Total Healthcare Expenditures, Hospitalizations, and Emergency Department Visits

Outcomes	Best Predictive Power				Second Best Predictive Power			
	Models		Estimates		Models		Estimates	
	No.	Predictors	Adj. R^2 (%)	*c* statistic	No.	Predictors	Adj. R^2 (%)	*c* statistic
Healthcare Expenditures								
1-year total exp.	3	Index-year exp.	35.62		5	CCI-2	11.54	
2-year total exp.	35	Index-year exp.	31.55		37	CCI-2	12.31	
1-year ≥ 90th percentile	19	Index-year exp.		0.810	18	# of meds		0.767
2-year ≥ 90th percentile	51	Index-year exp.		0.823	50	# of meds		0.771
Hospitalizations								
1-year # of admissions	69	CCI-2	8.05		68	CCI-1	6.87	
2-year # of admissions	101	CCI-2	9.26		100	CCI-1	8.06	
1-year risk of admissions	83	Index-year exp.		0.684	82	# of meds		0.677
2-year risk of admissions	115	Index-year exp.		0.676	114	# of meds		0.663
Emergency Department Visits								
1-year # of visits	130	# of meds	9.89		135	CCI-2	6.57	
2-year # of visits	162	# of meds	12.44		167	CCI-2	8.83	
1-year risk of visits	146	# of meds		0.653	151	CCI-2		0.624
2-year risk of visits	178	# of meds		0.654	183	CCI-2		0.626

Adj. R^2: adjusted R^2; # : number; exp.: expenditures

Note: All the models include age and sex as covariates

CCI-1 is based on Deyo RA, et al. "Adapting a Clinical Comorbidity Index for Use with ICD-9-CM Administrative Databases." *Journal of Clinical Epidemiology* 45, (1992): 613-19.

CCI-2 is based on Charlson ME, et al. "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients." *Journal of Clinical Epidemiology* 61, no. 12 (2008): 1234-40.

4.2 PREDICTION OF TOTAL HEALTHCARE EXPENDITURES

For the prediction of total healthcare expenditures over one year and two years, all six measures explained significant proportions of the variation after adjusting for age and sex, but the models that included the index-year healthcare expenditures ($model_3$; $model_{35}$) were considerably better than the other measures as they explained approximately one-third of the variance in future expenditures. In identifying the subgroup of individuals who incurred the highest ($\geq 90^{th}$ percentile) expenditures, the index-year healthcare expenditures ($model_{19}$; $model_{51}$) also appeared to have the best discriminatory power, although the models that included the number of distinct medications ($model_{18}$; $model_{50}$) exhibited the best calibration. In addition, the measures showed improved predictive power when the time horizon was extended from one year to two years. In model prediction studies, a *c* statistic value of less than 0.6 is considered as poor, between 0.7 and 0.8 as acceptable, and between 0.8 and 0.9 as excellent.[100] Based on the results from the logistic regressions, all six measures were acceptable or excellent predictors.

Contrary to the findings from the current study, two previous studies found the count of prescription medications to be a better predictor of healthcare expenditures than CCI-1 or CDS-1.[101,102] However, the definitions of "distinct" medications are different in

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100 David W. Hosmer Jr. and Stanley Lemeshow, *Applied Logistic Regression*, 2nd ed. (New York, NY: John Wiley & Sons, 2000).

101 Schneeweiss et al., "Performance of Comorbidity Scores to Control for Confounding in Epidemiologic Studies Using Claims Data."

these studies: in the current study, a drug is considered a distinct medication if it has a unique chemical structure, whereas in the other studies, two drugs in the same pharmacologic or therapeutic class would only be considered as one distinct medication. Therefore, direct comparison of the findings should be cautioned. Between the CCI-1 and CDS-1, the results from the current study are consistent with an earlier study, which found the CCI-1 to be a better predictor of healthcare expenditures than the CDS-1.[103]

Only two other studies have compared the predictive power of index-year healthcare expenditures with other comorbidity adjustment measures in explaining future expenditures. Farley et al. found the CCI-1 and the index-year expenditures to be similar in predicting future expenditures, but the count of prescription medications was the most powerful predictor.[104] In a diabetic Veterans population that was predominantly male, index-year expenditures performed similarly as the CCI-1 for the prediction of one-year healthcare expenditures, but neither of the measures explained more than four percent of the variation.[105] In comparison, the current study found the index-year healthcare expenditures to be the best predictor of future healthcare expenditures ($model_3$; $model_{35}$) and high-expenditure individuals ($model_{19}$; $model_{51}$). One explanation could be that the expenses incurred by the TRICARE beneficiaries are almost fully captured by the claims

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[102] Perkins et al., "Common Comorbidity Scores Were Similar in Their Ability to Predict Health Care Costs and Mortality."

[103] Onur Baser, Liisa Palmer, and Judith Stephenson, "The Estimation Power of Alternative Comorbidity Indices," *Value in Health* 11, no. 5 (2008).

[104] Farley, Harley, and Devine, "A Comparison of Comorbidity Measurements to Predict Healthcare Expenditures."

[105] Maciejewski, Liu, and Fihn, "Performance of Comorbidity, Risk Adjustment, and Functional Status Measures in Expenditure Prediction for Patients with Diabetes."

records because they only receive medical care through TRICARE or TRICARE-affiliated programs. However, this hypothesis cannot be tested in the current study.

4.3 PREDICTION OF HOSPITALIZATIONS

For the prediction of the **number** of hospitalizations, the CCI-2 ($model_{69}$; $model_{101}$) was the best predictor, but the index-year healthcare expenditures ($model_{83}$; $model_{115}$) performed the best in predicting the **risk** of hospitalizations (≥ one hospital admission). However, neither predictor showed good model fit. The range of *c* statistics in the current study was similar to those in previous studies: Perkins et al. found that the CCI-1, CDS-1, and the count of prescription medications had *c* statistic values between 0.636 and 0.670.[106] Similarly, Schneeweiss et al. found the range of *c* statistic values to be below 0.7 for the prediction of non-emergency and emergency hospitalizations.[107] Both studies found the number of prescription medications to be a better predictor than the CCI-1 or CDS-1, which is consistent with the findings from this study. However, since these two other studies did not evaluate the effect of index-year healthcare expenditures, the relative performance between the number of distinct medications and prior expenditures could not be ascertained. As mentioned earlier, the definition of distinct medications in this study is different from those in the two previous studies. Overall, the results from the current study confirm previous findings that comorbidity

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[106] Perkins et al., "Common Comorbidity Scores Were Similar in Their Ability to Predict Health Care Costs and Mortality."

[107] Schneeweiss et al., "Performance of Comorbidity Scores to Control for Confounding in Epidemiologic Studies Using Claims Data."

adjustment measures are poor predictors of the risk of hospitalization, as indicated by the low *c* statistic values.

4.4 PREDICTION OF EMERGENCY DEPARTMENT VISITS

In predicting the **number** and **risk** (≥ one visit) of emergency department visits, the number of distinct medications was the most powerful predictor ($model_{130}$; $model_{146}$; $model_{162}$; $model_{178}$). Augmenting the number of distinct medications with the other measures in the prediction models showed improved predictive power. Among the six measures, only the index-year expenditures models showed poor model fit ($model_{147}$; $model_{179}$). Overall, all the measures examined in the current study were poor predictors of risk of emergency department use. One explanation for why a simple count of distinct medications was a better predictor than either CDS-1 or CDS-2 in the study is that misclassification may have occurred. That is, a drug that is used for multiple indications may have been grouped to a different diagnosis incorrectly when matching medications to the listed diagnoses in the CDS. Little has been done to examine the utility of comorbidity adjustment measures in predicting emergency department visits. In one previous study, the CCI-1 was found to be not associated with non-urgent emergency department use among a group of type II diabetic patients.[108]

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[108] Shang-Jyn Chiou et al., "Use of the Emergency Department for Less-Urgent Care among Type 2 Diabeticss under a Disease Management Program," *BMC Health Services Research* 9 (2009).

4.5 Comparison of Medication-based with Diagnosis-based Measures

The results from this study imply that either diagnosis-based or medication-based comorbidity adjustment measures may be preferable depending on the outcome variable of interest. Based on the proportion of variation explained, the CCI-1 and CCI-2 seemed to be most predictive of total healthcare expenditures, followed by hospitalizations, and then emergency department visits. On the other hand, the CDS-1 and CDS-2 were most predictive of emergency department visits, followed by total healthcare expenditures and hospitalizations. However, while the CCI-1 and CCI-2 appeared to be better than the CDS-1 and CDS-2 in predicting the number of hospitalizations and total healthcare expenditures, a simple count of distinct medications was a better predictor of the number of emergency department visits than diagnosis-based measures.

Two competing hypotheses exist with regards to the relative performance of diagnosis-based and medication-based comorbidity adjustment measures.[109] One hypothesis is that diagnosis-based measures are superior to medication-based measures because diagnosis-based measures account for diagnoses untreated by drugs, and two conditions treated by the same drug (e.g., cancer and rheumatoid arthritis treated by methotrexate) would also be captured in the indices. The alternative hypothesis is that medication-based measures are superior because patients may only have their most relevant diagnoses coded in administrative claims data, and prescriptions filled by

[109] Schneeweiss et al., "Performance of Comorbidity Scores to Control for Confounding in Epidemiologic Studies Using Claims Data."

patients may be a better reflection of their true health status. However, the results from the current study support neither hypothesis.

It has been suggested that medication-based measures could be used in conjunction with diagnosis-based measures in the same prediction model to increase the model's explanatory power, as these two types of comorbidity adjustment measures may account for variation that is otherwise not measured. Results from the regression models in this study showed that combination models did exhibit better predictive power, but the improvements were limited. Furthermore, there appears to be a "ceiling effect" that could be achieved by incorporating several comorbidity adjustment measures in one single model: the CDS-1 and CDS-2 seemed to have limited effect on the predictive power of combination models that already include the number of distinct medications, total healthcare expenditures, and the CCI.

Even if the combination models result in increases in predictive power that are statistically significant, such improvements may have little practical significance. For the prediction of emergency department visits, the combination models examined in this study remained poor predictors as the *c* statistic values were below 0.7. Using more than one comorbidity adjustment measure in one study may not be ideal because it requires additional time and resources for coding and data analysis. In general, diagnosis-based measures are easier to use because medication-based measures such as the CDS require continued updates of new medications that are used to treat the specified chronic conditions. However, it should be noted that a simple count measure such as the number of distinct medication and a prior utilization measure such as the index-year total

healthcare expenditures were as good or better than the CCI or CDS in this study, and using these two alternative measures may be more efficient.

4.6 Comparison of the Original and the Updated Charlson Comorbidity Indices

At the time of this study, no other studies were found to have validated the utility of the updated Charlson Comorbidity Index (CCI-2) after it was developed. In the current study, the CCI-2 performed consistently better than the CCI-1 in predicting all outcome variables for diabetic patients. The improved performance is likely a result of the inclusion of additional diagnoses and medication use (depression, hypertension, skin ulcers, and the use of warfarin) that are not covered in the CCI-1. Previous studies have shown that depression is associated with increased healthcare costs in diabetic patients.[110,111] However, whether one or more of these additional risk factors contribute to the increased predictive power warrants further investigation. Among the four new risk factors in CCI-2, it may be of particular interest to examine whether eliminating the use of warfarin from the CCI-2 would significantly impact its predictive power. As pharmacy claims data may sometimes be unavailable to researchers, a "modified" CCI-2 that requires no prescription claims data may be useful in epidemiologic research. Overall, the findings from the current study suggest that, in a diabetic population under the age of 65,

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[110] Gregory E. Simon et al., "Diabetes Complications and Depression as Predictors of Health Service Costs," *General Hospital Psychiatry* 27 (2005).

[111] Egede, Zheng, and Simpson, "Comorbid Depression Is Associated with Increased Health Care Use and Expenditures in Individuals with Diabetes."

the CCI-2 should be considered in place of the CCI-1 when the outcomes of interest are total healthcare expenditures, hospitalizations, and emergency department visits.

4.7 Utility of Comorbidity Adjustment Measures

The six comorbidity adjustment measures examined in the current study showed varying degrees of predictive power, and the proportion of variation explained by these measures generally fell below 10 percent. The results suggest that these measures may be a useful tool to control for confounding in administrative database research, but the effects are limited. There are several reasons why comorbidity adjustment measures only have limited explanatory power in predicting health services utilization:

First, administrative claims databases are designed for billing purposes but not for use with comorbidity adjustment measures. That is, such databases may reflect the intensity of resource utilization more accurately than they reflect a patient's health status. As an example, for medication-based measures such as the CDS, if the physician does not prescribe medications for a medical condition or if the patient does not fill the prescribed medication, then the CDS will not be able to detect the medical condition. For diagnosis-based measures such as the CCI, a patient's comorbid conditions may not be fully captured because the conditions may not be relevant to the principal diagnosis when the patient receives medical care and thus not recorded in the claims. In other words, the predictive power of comorbidity adjustment measures is limited by the available data.

Second, both versions of the CCI and the CDS were originally developed from patient cohorts of different disease states to predict several different outcomes, and previous literature indicates that the performance of comorbidity adjustment measures varies when different patient populations or outcomes are examined. The CCI-1 was derived from a cohort of breast cancer patients to predict one-year mortality, and the CCI-2 was developed from a group of primary care patients to predict annual healthcare costs. Thus, the calibrations of weights in these two indices were a function of the outcomes under investigation and the distribution of chronic diseases in the patient populations. This is also true for the CDS-1 and CDS-2. It is likely that a chronic condition that is highly predictive of mortality may not predict healthcare expenditures well, and vice versa. The findings from the current study support the hypothesis that comorbidity adjustment measures could be more predictive of one health outcome over another.

Third, the measures examined in this study were designed for use in general populations, and chronic conditions that are more relevant to diabetic patients may have been omitted in these indices. Young et al. developed a Diabetes Complications Severity Index (DCSI) that uses both diagnosis codes and laboratory data to identify seven diabetes-related complications, including retinopathy, nephropathy, neuropathy, cerebrovascular complications, cardiovascular complications, peripheral vascular disease, and metabolic complications.[112] The DCSI was shown to be a slightly better predictor of

[112] Bessie Ann Young et al., "Diabetes Complications Severity Index and Risk of Mortality, Hospitalizations, and Healthcare Utilization," *The American Journal of Managed Care* 14, no. 1 (2008).

mortality and hospitalization than a simple count of medications.[113] However, when compared with the CCI and other comorbidity adjustment measures, the DCSI had very poor predictive power in predicting healthcare expenditures.[114] The reason could be that the DCSI only accounts for a limited range of diabetes-related complications but not other comorbidities that may be highly associated with healthcare expenditures.

The performance of prediction models is often evaluated using the area under the receiver-operator curve, or the *c* statistic, which indicates a model's discriminatory power. However, one should interpret the c statistic cautiously because it is only a function of how well a model can rank order cases versus non-cases, but it does not reflect the magnitudes of the differences in rank. For example, the *c* statistic does not differentiate between individuals who have CCI scores of two and five if they are both compared to individuals who have a CCI score of zero: in this case, perfect discrimination is achieved because individuals with scores of two and five are treated as cases, and individuals with a score of zero are treated as non-cases. However, in the clinical setting, a patient with a CCI score of five may be significantly sicker than a patient with a CCI score of two and thus warrant additional medical attention or different treatment recommendations. Therefore, a model's calibration should also be taken into consideration when evaluating model performance as it indicates how well the predicted distribution of cases matches the observed distribution.

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[113] Ibid.

[114] Maciejewski, Liu, and Fihn, "Performance of Comorbidity, Risk Adjustment, and Functional Status Measures in Expenditure Prediction for Patients with Diabetes."

In this study, model calibration was tested using the Hosmer-Lemeshow goodness-of-fit chi-square test, where a statistically significant chi-square value indicates lack of model fit and poor calibration. For the prediction of one-year risk of hospitalization, the number of distinct medications and index-year healthcare expenditures showed similar discriminatory power based on the c statistics, but the model that included the number of distinct medications had better model fit. In this case, the number of distinct medications may be a more ideal adjuster for comorbidity than the index-year expenditures. To date, model calibration receives relatively little attention in risk model comparison studies, but the utility of comorbidity adjustment measures should be assessed based on both the discrimination and calibration of the prediction model.

4.8 LIMITATIONS OF THE STUDY

The results from this study should be interpreted in light of the following limitations:

First, the study results may have been biased toward patients who had been hospitalized. In the TRICARE claims database, a total of up to 20 ICD-9-CM fields may be recorded in the inpatient setting, while only a maximum of eight ICD-9-CM fields may be recorded for an outpatient visit. Therefore, it is likely that patients who were hospitalized incidentally had more diagnoses captured in the database. As such, these patients may have accounted for individuals who produced higher comorbidity scores. However, the distributions of scores derived from the comorbidity adjustment measures

in this study appeared similar to those in previous literature, with the majority of the patients at the lower end of the spectrum and a few patients with outlying high values.

Second, the study findings may not be generalizable to other patient populations. The Department of Defense TRICARE population may not be representative of patient populations who receive care through other insurers. The study population is limited to people under the age of 65 who had type I or II diabetes and received care for their diabetes.

Third, expenses incurred outside the TRICARE system were not captured by the claims data. As such, the predictor and outcome that included the sum of healthcare expenditures may have been underestimated. However, results from the current study indicated that the index-year expenditures appeared to be a robust predictor of healthcare utilization and expenditures.

Fourth, coding practices may be different across hospitals and clinics within the TRICARE system, resulting in inconsistencies in data quality. The claims data may also be incomplete, as only the most relevant and current diagnoses may be recorded at an ambulatory visit or hospital admission. Inaccuracy of administrative coding systems may be a concern, including both false-positive and false-negative records of diagnoses and prescription fills. However, automated databases have been shown to be an efficient way to identify comorbidities and complications of diabetes for epidemiologic and health services research.[115]

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[115] Katherine M. Newton et al., "The Use of Automated Data to Identify Complications and Comorbidities of Diabetes: A Validation Study," *Journal of Clinical Epidemiology* 52, no. 3 (1999).

Fifth, certain demographic and clinical variables were not available for this study, such as race, ethnicity, duration of diabetes, and body mass index. These risk factors may be important predictors of healthcare utilization and expenditures for diabetic patients.

4.9 Conclusions and Recommendations for Future Research

Comorbidity adjustment measures are used for different purposes in epidemiological research. They can be used to correct for confounding or predict study outcomes. As such, the purpose of their use may dictate when and whether a particular measure should be used. Although the CCI and CDS seemed to have limited power to predict hospitalizations and emergency department visits, researchers may still consider using these measures to adjust for comorbidity to accurately measure the associations between the independent and dependent variables. Nevertheless, prior utilization such as the index-year healthcare expenditures could be a more powerful predictor of future healthcare expenditures, and simple count measures such as the number of distinct medications could be a more efficient way to adjust for comorbidity. The CCI-2 also appeared to have better predictive power than the CCI-1 for use in a diabetic population.

Suggestions for future research include:

1) developing diabetes-specific comorbidity adjustment measures to improve comorbidity adjustment for diabetic patients;
2) improving existing comorbidity adjustment measures by recalibrating scoring algorithms for use in different disease states;

3) validating the updated Charlson Comorbidity Index for use in different patient populations and for different health outcomes; and

4) assessing the performance of diagnosis-based and medication-based measures with prior utilization and simple count measures such as the number of prescription medications or the number of chronic conditions.

Appendix A. Charlson Comorbidity Index – Weights, Diagnoses and the Deyo, Dartmouth-Manitoba, and D'Hoore ICD-9 Codes

Weight	Diagnoses*	Deyo codes†	Dartmouth-Manitoba codes‡	D'Hoore codes§
1	Myocardial infarction	410.xx, 412	410.xx, 412	410, 411
1	Congestive heart failure	428.x	402.01, 402.11, 402.91, 425.x, 428.x, 429.3	398, 402, 428
1	Peripheral vascular disease	441.x, 443.9, 785.4, V43.4, 38.48(P)	440.x, 441.x, 442.x, 443.x, 447.1, 785.4, 38.13(P), 38.14(P), 38.16(P), 38.18(P), 38.33(P), 38.34(P), 38.36(P), 38.38(P), 38.43(P), 38.44(P), 38.46(P), 38.48(P), 39.22(P), 39.23(P), 39.24(P), 39.25(P), 39.26(P), 39.29(P)	440-447
1	Cerebrovascular disease	430-437.x, 438	362.34, 430-436, 437-437.1, 437.9, 438, 781.4, 784.3, 997.0, 38.12(P), 38.42(P)	430-433, 435
1	Dementia	290.x	290.x, 331-331.2	290, 291, 294
1	Chronic pulmonary disease	490-496, 500-505, 506.4	415.0, 416.8-416.9, 491.x-494, 496	419-493
1	Ulcer disease	531.4x-531.7x, 532.4x-532.7x, 533.4x-533.7x, 534.4x-534.7x, 531.0x-531.3x, 532.0x-532.3x, 533.0x-533.0x, 534.0x-534.3x, 531.9, 532.9, 533.9, 534.9	531.xx-534.xx	531-534

Weight	Diagnoses	Deyo codes	Dartmouth-Manitoba codes	D'Hoore codes
1	Mild liver disease	571.2, 571.4, 571.5, 571.6	571.2, 571.5-571.6, 571.8-571.9	571, 573
1	Diabetes	250.0x-250.3x, 250.7x	250.0x-250.3x	N/A
1	Connective tissue disease	N/A	N/A	710, 714, 725
2	Hemiplegia	342.x, 344.1	342.x, 344.x	342, 434, 436, 437
2	Moderate or severe renal disease	582.x, 583.0-583.7, 585, 586, 588.x	585-586, V42.0, V45.1, V56.x, 39.27(P), 39.42(P), 39.93-39.95(P), 54.98(P)	403, 404, 580-586
2	Diabetes with end organ damage	250.4x-250.6x	250.4x-250.9x	250
2	Any tumor	140.x-172.x, 174.x-195.x, 200.x-208.x	140.x-171.x, 174.x-195.x, 200.xx-208.x, 273.0, 273.3, V10.46, 60.5(P), 62.4-62.41(P)	140-195
2	Leukemia			204-208
2	Lymphoma			200, 202, 203
3	Moderate or severe liver disease	572.2-572.8	572.2-572.4, 456.0-456.2x, 39.19(P), 42.91(P)	070, 570, 572
6	Metastatic cancer	196.x-199.x	196.x-199.x	196-199
6	AIDS	042.x-044.x	N/A	N/A

ICD-9: The International Classification of Diseases, 9th Revision; N/A: Not Applicable; AIDS: Acquired Immunodeficiency Syndrome

(P) indicates ICD-9 procedure codes

[*] Charlson, Mary E., Peter Pompei, Kathy L. Ales, and C. Ronald MacKenzie. "A New Method of Classifying Prognostic Comorbidity in Longitudinal Studies: Development and Validation." *Journal of Chronic Diseases* 40, no. 5 (1987): 373-83.

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Appendix B. Updated Charlson Comorbidity Index – Additional Conditions, Weights, ICD-9 Codes, and GCN Codes

Weight	Diagnoses	ICD-9 codes	GCN codes
1	Depression	296.2x-296.3x, 311.x	N/A
1	Use of warfarin	N/A	25790-25798
1	Hypertension	401.x	N/A
2	Skin ulcers/cellulitis	682.x, 707.x	N/A

ICD-9: The International Classification of Diseases, 9th Revision; GCN: Generic Code Number; N/A: Not Applicable

* These diagnoses are included in Charlson et al.'s 2008 adaptation: "The Charlson Comorbidity Index Is Adapted to Predict Costs of Chronic Disease in Primary Care Patients." *Journal of Clinical Epidemiology* 61, no. 12 (2008): 1234-40.

Appendix C. Chronic Disease Score – Conditions, Medication Classes, and Weights

Conditions	Medication class or classes	Weight
Heart disease	(1) Anti-coagulants, hemostatics (2) Cardiac agents, ACE inhibitors (3) Diuretic loop	One class = 3 Two classes = 4 Three classes = 5
Respiratory illness	(1) Isoproterenol (2) Beta-adrenergic, miscellaneous (3) Xanthine products (4) Respiratory products including bronchodilators and mucolytics but excluding cromolyn (5) Epinephrine	One class = 2 Two or more classes = 3
Asthma, rheumatism	Glucocorticoids	Score = 3
Rheumatoid arthritis	Gold salts *Systemic corticosteroids* *Hydroxychloroquine* *Methotrexate* *DMARDs* *Anti-TNFs*	Score = 3
Cancer	Antineoplastics	Score = 3
Parkinson's	L-Dopa *Selegiline* *Adamantanes* *Anticholingergic agents* *COMT inhibitors* *Dopamine receptor agonists*	Score = 3
Hypertension	(1) Antihypertensives (except ACE inhibitors) or calcium channel blockers (2) Beta blockers, diuretics	If class (1) = 2 If class (2) and not (1) = 1
Diabetes	Insulin, oral hypoglycemics	Score = 2
Epilepsy	Anticonvulsants	Score = 2
Asthma, rhinitis	Cromolyn *Leukotriene modifiers*	Score = 2
Acne	(1) Antiacne tretinoin (2) Topical macrolides	Either class with two or more prescriptions filled = 1
Ulcers	Cimetidine	Score = 1
Glaucoma	Ophthalmic miotics	Score = 1

Conditions	Medication class or classes	Weight
Gout, hyperuricemia	Uric acid agents	Score = 1
High cholesterol	Antilipemics	Score = 1
Migraines	Ergot derivatives	Score = 1
Tuberculosis	Antitubercular agents	Score = 1

ACE: Angiotensin Converting Enzyme
L-Dopa: 3,4-dihydroxy-L-phenylalanine
DMARDs: Disease-modifying antirheumatic drugs
Anti-TNFs: Anti-tumor necrosis factors
COMT inhibitors: Catechol-O-methyl transferase inhibitors
Medications in *italics* are drugs that became available after the Chronic Disease Score was developed 1992. These drugs were included in the study for the calculation of the Chronic Disease Score.
[*] Von Korff, Michael, Edward H. Wagner, and Kathleen Saunders. "A Chronic Disease Score from Automated Pharmacy Data." Journal of Clinical Epidemiology 45, no. 2 (1992): 197-203

Appendix D. Chronic Disease Score – Explanatory Variables, Medication Classes, and Weights for Prediction of Total Cost, Outpatient Cost, and Primary Care Visits

Variable	Medication class or classes	Weights		
		Total cost	Out-patient cost	Primary care visits
Intercept		2011.4	539.0	1.44
Age (year)				
18-24		-1684.8	-283.7	-0.41
25-34		-1592.7	-215.8	-0.24
35-44		-1704.8	-239.3	-0.29
45-54		-1616.4	-208.8	-0.24
55-64		-1418.2	-147.5	-0.20
65-74		-967.0	-24.9	-0.06
75-84		-505.3	27.2	0.18
85+		0.0	0.0	0.00
Male		-74.3	-108.2	-0.33
Coronary and peripheral vascular disease	Anticoagulants, Pentoxifylline, Ticlopidine, *Platelet-aggregation inhibitors, Dypyridamole*	1932.3	587.3	0.61
Epilepsy	Anticonvulsant barbiturates & congeners, Phenytoin & combinations, Miscellaneous anticonvulsants, *Benzodiazepines, Succinimides*	771.5	402.2	0.29
Hypertension	ACE inhibitors, Alpha blockers, Antihypertensive vasodilators, Beta-adrenergic blockers, Calcium channel blockers, Clonidine, Thiazide diuretics, Ganglionic blockers, Guanethidine, Methyldopa, Rauwolfia alkaloids, *Nitrates and nitrites,*	64.3	84.0	0.34

Variable	Medication class or classes	Weights		
		Total cost	Out-patient cost	Primary care visits
	Dihydropyridines, *Direct vasodilators,* *Miscellaneous vasolidating agents*			
Tuberculosis	Antitubercular antibiotics, *Miscellaneous antimycobacterials*	5109.8	834.0	0.59
Rheumatoid arthritis	Systemic corticosteroids, Gold salts, Hydroxychloroquine, *Methotrexate,* *DMARDs,* *Anti-TNFs*	1199.6	454.6	0.71
HIV	Zidovudine, Didanosine, Zalcitabine, Pentamidine, Clarithromycin, Rifabutin, Atovaquonem, *HIV entry and fusion inhibitors,* *Protease inhibitors,* *Integrase inhibitors,* *Nonnucleoside reverse transcriptase inhibitors,*	4853.2	2368.7	3.53
High cholesterol	Antilipemics, *Cholesterol absorption inhibitors,* *Fibric acid derivatives,* *Miscellaneous antilipemic agents*	293.4	302.1	0.32
Malignancies	Antineoplastics, Colony-stimulating factors, Miscellaneous antinausea agents, Ondansetron	1940.2	903.6	-0.10
Parkinson's disease	Autonomics L-Dopa, Selegiline, *Adamantanes,* *Anticholinergic agents,* *COMT inhibitors,* *Dopamine receptor agonists*	2114.4	1155.6	0.45
End-stage renal disease	Marrow stimulants, Erythropoietin	2192.8	3196.7	-1.17

Variable	Medication class or classes	Weights		
		Total cost	**Out-patient cost**	**Primary care visits**
Heart disease	Beta-adrenergic blockers, Calcium channel blockers, Disopyramide, Vasodilator nitrates, Digitalis glycosides, Loop diuretics, Procainamide, Quinidine, Class 1A, 1C, 1I antiarrhythmics	789.1	230.2	0.40
Diabetes	Insulins, Sulfonylureas, *Alpha-glucosidase inhibitors,* *Amylinomimetics,* *Biguanides,* *Dipeptidyl peptidase IV inhibitors,* *Incretin mimetics,* *Meglitinides,* *Thiazolidinediones,*	1108.4	423.9	0.91
Glaucoma	Diuretic carbon-anhydrase inhibitors, Ophthalmic beta blockers, Ophthalmic miotics, *Alpha-adrenergic agonists,* *Prostaglandin analogs*	351.7	330.7	0.18
Cystic fibrosis	Mucolytics, Pancreatic enzymes	2341.6	365.6	0.10
Renal failure	Potassium removing resins, Kayexalate	16579.0	1675.1	-0.46
Liver failure	Ammonia detoxicants	1519.1	798.5	0.33
Ulcers	Histamine H_2 blockers, Prostaglandin, Misoprostil, Proton pump inhibitors, Omeprazole, *Protectants*	797.1	351.1	0.54
Transplants	Cyclosporine-A, Azathioprine	3411.6	2733.5	-0.99
Respiratory illness, asthma	Beta agonist bronchodilators, Xanthines,	561.2	262.3	0.60

Variable	Medication class or classes	Weights		
		Total cost	Out-patient cost	Primary care visits
	Cromolyn, Inhaled corticosteroids, *Leukotriene modifiers*			
Thyroid disorders	Thyroid replacement antithyroid agents	282.8	135.5	0.23
Gout	Colchicine, Uric acid inhibitors	833.8	146.2	0.07
Crohn's disease & inflammation of bowel	Sulfasalazine, Olsalazine, Mesalamine	614.7	281.8	0.14
Pain and inflammation	Nonsteroidal anti-inflammatory drugs	137.6	145.7	0.48
Depression	Tricyclic antidepressants, Monoamine oxidase inhibitors, Selective serotonin reuptake inhibitors, *Selective serotonin- and norepinephrine-reuptake inhibitors,* *Serotonin modulators,* *Miscellaneous antidepressants*	545.4	385.9	0.67
Psychotic illness	Butyrophenones, Phenothiazines, Miscellaneous antipsychotics, Thiothixene, Atypical antipsychotics	1438.7	466.7	0.50
Mania	Lithium	260.1	416.9	0.32
Anxiety, tension	Benzodiazepines, Meprobamate, Miscellaneous antianxiety agents	480.0	292.1	0.52
Pain	Narcotics Opiate partial agonists	633.2	261.8	0.46

ACE: Angiotensin Converting Enzyme
L-Dopa: 3,4-dihydroxy-L-phenylalanine
COMT inhibitors: Catechol-O-methyl transferase inhibitors
DMARDs: Disease-modifying antirheumatic drugs
Anti-TNFs: Anti-tumor necrosis factors
Medications in *italics* are drugs that became available after the Chronic Disease Score was developed 1995. These drugs were included in the study for the calculation of the Chronic Disease Score.

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