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Hua Hao Date

Medicaid Coverage and Nephrology Care Influence Patient Mortality among United States Dialysis Facilities

By

Hua Hao

MPH

Epidemiology

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Rachel Elizabeth Patzer, PhD

Committee Chair

_____

Howard H. Chang, PhD

Committee Member

Medicaid Coverage and Nephrology Care Influence Patient Mortality among United States Dialysis Facilities

By

Hua Hao

Bachelor of Science

Macau University of Science and Technology

2011

Thesis Committee Chair: Rachel Elizabeth Patzer, PhD

An abstract of

A thesis submitted to the Faculty of the
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Abstract

Medicaid Coverage and Nephrology Care Influence Patient Mortality among United States Dialysis Facilities

By Hua Hao

Background: Pre-ESRD nephrology care is important for better clinical outcomes for patients with end stage renal disease (ESRD). Timely receipt of nephrologist care is associated with slower chronic kidney disease (CKD) progression, lower rates of adverse outcomes, higher survival, and improved quality life. Delayed care is associated with progression of kidney disease and increased mortality after start of hemodialysis. Prior studies suggest that patient socioeconomic status may be an indicator for late nephrologist referral. The aim of this study was to determine the association between pre-ESRD nephrology care and standardized mortality ratio among dialysis facilities in the US, and to determine whether this association varied by Medicaid health insurance coverage.

Methods: A total of 5,387 dialysis facilities were identified from the Dialysis Facility Report data from 2007-2010, which presented detailed data from the ESRD Medical Evidence Form (FORM CMS-2728) across 18 dialysis facility networks (56 states and territories) in the U.S. Receipt of pre-ESRD nephrology care was based on the CMS 2728 Medical Evidence Form which was completed for all ESRD patients at the time of ESRD start. Standardized mortality ratio (SMR) was calculated as the number of observed deaths within a dialysis facility over the number of expected deaths within a facility. A marginal mixed generalized estimating equation model assuming exchangeable covariance structure was used to estimate the association between pre-ESRD nephrology care and facility SMR as well as effect modification of Medicaid coverage.

Results: The percentage of patients who received pre-ESRD nephrology care within a facility was significantly associated with facility-level SMR. In particular, for a ten percent increase in pre-ESRD nephrology care, facility SMR decreased 1.30% (95% CI, 0.90%-1.61%). Compared to facilities whose proportion of patients received Medicaid coverage (MC) greater than the third quartile, facilities whose MC lower than the first quartile experienced a significant 1.10% (95% CI, 0.10%-2.10%) increase in rate of change between pre-ESRD nephrology care and facility SMR.

Conclusion: As the percentage of patients who received pre-ESRD nephrology care within a facility increased, the facility-level SMR decreased. This association was modified by patient Medicaid coverage, where a decreased proportion of patients who received Medicaid Coverage resulted in a steeper rate of change. These results suggested that targeted quality improvement interventions to improve access to pre-ESRD nephrology care could reduce mortality among ESRD patients in dialysis facilities.

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Medicaid Coverage and Nephrology Care Influence Patient Mortality among United States Dialysis Facilities

CHAPTER 1-LITERATURE REVIEW AND INTRODUCTION

Introduction

This chapter provides a review of the literature on chronic kidney disease (CKD) that examines the nature and effects of chronic kidney disease and pre-End Stage Renal Disease (ESRD) nephrology care. Specifically, the literature review summarizes current findings on potential confounders, effect modifiers, and methodology for evaluating relationships between pre-ESRD nephrology cares, Medicaid coverage, and mortality among dialysis facilities in the United States.

Chronic Kidney Disease

Definition

The National Kidney Foundation Work Group defines CKD to include conditions affecting the kidney, that have the potential to cause either progressive loss of kidney function or complications resulting from decreased kidney function. Chronic kidney disease is thus defined as the presence of kidney damage or decreased level of kidney function for three months or more, regardless of diagnosis. [1]

Specifically, when CKD progresses into the fifth stage, it will result to end stage renal disease (ESRD). ESRD is when kidney stop working well enough for you to live without dialysis or transplant. This kind of kidney failure is permanent and cannot be fixed. [1]

Morbidity and Mortality

Morbidity and mortality resulting from chronic kidney disease are incontestable. Globally, the number of patients with end-stage renal disease (ESRD) is increasing steadily. Currently, there are more than 1.6 million individuals undergoing renal replacement therapy (RRT) with 34.4% hemodialysis. [2] In United States, according to the National Health and Nutrition Examination Survey (NHANES) 1999-2004, 16.8% of the U.S. population aged ≥20 years had CKD compared with 14.5% from 1988-1994, an increase of 15.9% based on crude estimates of prevalence. [3] A recent study reported that currently nearly 26 million Americans suffer from CKD [4] and future projections for the US population estimate there will be more than 700,000 prevalent cases of ESRD by the year 2015[5]. The mortality among CKD patients in 2009 was 56% greater among non-CKD patients after adjusting for age, gender, race, comorbidity, and prior hospitalizations. [6] Untreated CKD can results in end-stage renal disease or even death [3]. For example, the adjusted rate in patients with CKD of Stage 4-5 is 76% greater than that in non-CKD patients [6]. The decreased quality of life and increased health-care expenditures are burdens for not only the patient but also the U.S. health system.

Progression and Stage of CKD

Stage	Description	GFR (ml/min/1.73m2)
1	Kidney damage with normal or ↑GFR*	≥90
2	Kidney damage with mild ↓GFR	60-89
3	Moderate reduction in GFR	30-59
4	Sever reduction in GFR	15-29
5	Established kidney failure	<15 (or dialysis)

*GFR: Glomerular Filtration Rate

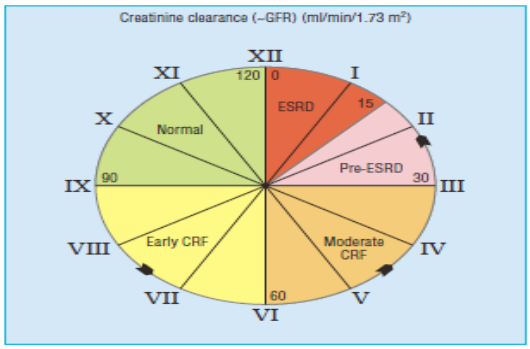

Fig 1 Continuum of renal disease (anticlockwise model) (CRF=chronic renal failure; ESRD=end stage renal disease; GFR=glomerular filtration rate)

Predictors of CKD

- Age: CKD is more prevalent in older individuals. In high-risk populations, relative mortality risk for reduced estimated glomerular filtration rate (eGFR) decreased with increasing age [7].
- Diabetes: Diabetes is a common cause of chronic renal failure and accounts for a large part of the growth in end stage renal disease in North America [8]. In general and high-risk cohorts, mortality risks were 1.2-1.9 times higher for patients with diabetes than for those without diabetes across the range of eGFR and albumin-to-creatinine ratio (ACR) [9].
- Hypertension: Hypertension is a well-established cause, a common complication, and an important risk factor for progression of renal disease. All caused mortality risk was 1.1-1.2 times higher in individuals with hypertension than in those without hypertension at preserved eGFR [10].
- Cardiovascular Disease: Cardiovascular disease is a common progression factor that can cause decline in renal function after onset of kidney damage. People with available information on the stage of chronic kidney disease or even without manifest vascular diseases are associated with excess risk of subsequent coronary heart disease [11].

- Tobacco Smoke: Smoking, besides increasing the risk of cardiovascular events, is an independent risk factor for development of ESRD in men with kidney disease. [12-13] Smoking cessation alone may reduce the risk of disease progression by 30% in patients with type 2 diabetes. [14]
- Late Nephrology Referral: Improved clinical results may be achieved if timely nephrologist referral leads to better management of comorbidities and slower CKD progression. Upon transition to ESRD, later nephrologist referral patients have been associated with greater short-term morbidity and worse metabolic status [15-20].
- Other Factors: Other factors such as race, ethnicity and socioeconomic status also influence the development and progression of CKD. African American and Hispanics in the United States have consistently been found to have higher prevalence of CKD than whites. [21] Female gender was associated with higher risk of CKD compared with males. [22-23] Also, the body mass index's (BMI) influences on the survival of CKD patients [24].

Economic Burden of Chronic Kidney Disease

Currently, approximately 485,000 Americans have been diagnosed with kidney failure and required ongoing, expensive and life-altering treatments, such as frequent dialysis treatment or kidney transplantation-to stay alive. This number is expected to grow to 785,000 by 2020. Nationally, the annual cost of treating ESRD is currently over $32 billion. [25] For individual patient, an average expense is $70,000k per year [26-27].

Because of the percentage of population exposed to CKD is large (greater than 10%, or more than 20 million, among aged 20 years or older in United States) and the associated costs of the

effects of exposure are substantial, Trivedi et al. developed a mathematical model to access what the impact of reduction in the rate of change in GFR would have on the incidence, prevalence and costs associated with CKD. If the rate of GFR decline by 10%, 20% or 30% in Stage 4-5 CKD patients beginning December 31, 1999, the decrease in prevalence of ESRD by 2020 would result in cumulative health care savings of approximately $9.06, $19.98, and $33.37 billion, respectively, according to their calculation. [28]

Summary

In summary, studies that measure the economic burden and the burden of death and disease attributed to CKD for the development of control risk factors which could increase the risk of kidney disease and prevent interventions for decline progression in renal function after onset of kidney damage are important.

Pre-ESRD Nephrology Care

Definition

Nephrology care before starting hemodialysis (HD) or patients who have received an Erythropoiesis-Simulating Agents (ESA) prior to end stage renal disease (ESRD) is defined as pre-ESRD nephrology care by no nephrology care, <6 months of care, 6-12 months and >12 months nephrology care [29].

Pre-ESRD Nephrology Care and Nephrologist Referral

According to United States Renal Date System (USRDS), 39% of hemodialysis patients reported they were first seen by a nephrologist three months or less prior to starting dialysis and 26% reported they were seen less than one month prior. Patients that have not seen or a nephrologist

prior to ESRD are less likely to know their therapeutic options or to select any other therapy. Therefore, early nephrologist referral is consistent with a higher probability of receiving earlier pre-ESRD nephrology care and there is little question that optimal pre-ESRD involves early detection. [30]

Significance

Pre-ESRD nephrology care from physicians, or specialists, including nephrologist and dietitians or early nephrology referral, was important for better clinical outcomes for patients with late stage CKD [31]. Jones C. et al found that following early nephrology referral, GFR declined more slowly and was associated with better survival. [32] Timely receipt of nephrologist care was also associated with slower CKD progression, lower rates of adverse outcomes, and improved quality of life [33]. The most recent review by Smart NA at el based on 3 database and 27 longitudinal cohort studies concluded that reduced mortality and hospitalization were associated with early nephrology referral [34] For patients with advanced CKD, nephrologist care increased the likelihood of receiving kidney transplantation. [35] Moreover, the expenses increased with CKD progression and these expenses increased dramatically as patients approach ESRD and remain elevated thereafter [36-40]. Robbins et al. estimated the magnitude of costs during the postdialysis period ($15,399 for 2-3 months after dialysis initiation) to be over three times higher and the peridialysis period ($35, 292 for the 30 days before and after initiation) to be over seven times higher than the predialysis period ($4265 for the 6-2 months prior). [38] Therefore, U.S. and international practice guidelines recommend that all patients with stage 4 and 5 CKD should be under nephrologist care [41-42].

Prevalence

Up to 25%-50% of patients undergoing maintenance dialysis in the United States have not received any pre-ESRD nephrologist care at all. [42] Older age, the existence of multiple comorbidities, geographic area, race other than Caucasian, lack of health insurance, lower socioeconomic status and education levels were patient characteristics that have been found to influence access to late pre-ESRD nephrologist care or late nephrology referral. [43-44] McClellan W. et al even stated that dialysis facilities in ESRD Network 5, 6, 8 and 11 yield an increased mortality. [45]

Previous Relevant Study Methodology and Result for Evaluating the Association between CKD mortality or survival and Pre-ESRD Nephrology Care or Early Nephrology Referral

In order to further understanding the association between CKD and pre-ESRD care or early nephrology referral based on previous studies, especially on the study design, study population, adjusted variables and statistical analysis, a review of the literature using the PubMed database and previous systematic reviews was conducted [46-47]. Of all retrieved results, only those involving adults with CKD published between 1990 and 2010 were examined. Relevant studies were organized into tables for further analysis.

Study	Study Design/population: NR (Criteria)	Statistical Analysis	Adjusted Variables	Important outcomes
Schmidt et al. 1998 48]	Retrospective cohort study of patients (n=238) beginning dialysis (1990 and 1997) in three dialysis units; LNR (<30 days of needing dialysis)	-Chi-square test -no modeling strategy	Age and cause of ESRD	-LR was not associated with lack of insurance or distance from referral site. -After controlling for age and cause of ESRD, there was no statistically significant difference in long-term survival between ER and LR patients.
Roubicek et al. 2000 [49]	Retrospective cohort study of patients (n=270) between 1989 and 1996 in one dialysis center. LNR (<16 weeks before dialysis)	-Cox hazards regression model	Age, sex, past history of hypertension, initial nephrology, comorbidity, referral pattern, need for emergent dialysis and albuminuria at start of dialysis	-ER was associated with greater risk for death -long term outcome of hemodialysis patients was not modified by delayed nephrology care
Astor et al. 2001[50]	Retrospective cohort study of patients (n=356) in one dialysis center. LNR(<30 days starting hemodialysis therapy)	-multivariate logistic regression	Age, sex, race, marital status, education, insurance coverage, comorbid disease status, albumin level, body mass index and underlying renal diagnosis.	-Arteriovenous (AV) vascular access at the initiation of treatment could prevent the need complication-prone dialysis catheters. -NR>4 months were more likely to have an AVF at dialysis (45% vs. 31%)
Stoves et al. 2001[51]	Retrospective cohort study of ESRD patients (n=1260) in single center. LNR(<=90 days)	-Cox hazards regression model -multivariate linear regression		-Survival at 4 months, 1 year and 5 years after dialysis initiation: LNR survival: 87%, 74% and 31% ENR survival: 94%, 87% and 55% -Age, diabetes, predialysis serum albumin, suitability for transplant work-up and transplant-ability and the interval between referral and dialysis were significant predictors for survival.
Avorn et al. 200 [52]	Retrospective cohort study of ESRD failure patients (n=2398) in New Jersey between 1991 and 1996. LNR (<=90 days)	-Multivariate logistic regression	Age, gender, race, socio-economic status (whether the patient had been enrolled in Medicaid or PPAD during the period) and the frequency and timing visits with a nephrologist.	-LNR associated with 42% increase to require central venous access for hemodialysis

Winelmayer et al. 2002 [53]	Matched case-control study of 32 transplant cases and 197 controls between 1991-1996 in New Jersey. (LNR<=90 days)	-conditional logistic regression		-LNR was associated with lower rate of renal transplantation (OR=0.22) and lower social economic status (indicated by enrollment in Medicaid or other state program for the poor) (OR=0.18) and comorbidity status (OR=0.69).
Jungers et al. 2002 [54]	Observational single center study of patients initiating dialysis (n=1057) and evaluated for pre-ESRD care duration and long-term outcome			-Prolonged nephrology pre-dialysis care is associated with better preserved CV condition, resulting in lower cardiovascular disease (CV) mortality on dialysis.
Kinchen et al. 2002 [55]	National prospective cohort study of 828 patients with new-onset ESRD within 81 dialysis facilities. (LNR<4 months)	-Cox Hazards regression -sensitivity analysis to address missing data	Sex, type of dialysis, smoking, exercise, comorbid conditions and disease severity and lab values	-Late evaluation of patients with chronic renal failure by a nephrologist is associated with greater burden and severity of comorbid disease, black ethnicity, lack of health insurance and shorter duration of survival.
Lhotta et al. 2002 [56]	Retrospective cohort study of patients (n=75) in single hospital between 1999 to 2000. (LNR defined as GFR<20mL/min/1.73 m2)	-logistic regression	Age, comorbidity status	-In univariate analysis, LNR patients only trended towards higher mortality (p=0.076) -In multivariate analysis, comorbidity was the only significant correlated variable.
Kessler et al. 2003 [57]	Prospective community based study in 2 years of patients (n=502)	-Multivariate logistic regression -cox Hazards regression	Age, cardiac disease with previous heart failure, vascular disease, low diastolic blood pressure, diabetes	-Risk of death compared with NR >12 months • NR 12-5 months 2.7 • NR 4-2 months: 2.8 • NR 1-0 months : 5.0
Schwenger et al. 2003[58]	Retrospective study of NR timing in Department of Medicine in Heidelberg and Vienna of patients (n=280) with ENR (>17 weeks before dialysis) vs. LNR	-Kaplan-Maier analysis of patients		-0-12 month mortality for ENR, LNR: 34.2%, 5.5% -12-24 month mortality for ENR, LNR: 15.3%, 11.4%
Lin et al. 2004 [59]	Retrospective cohort study of dialysis patients (n=78) (LNR<6 months)	-Kapan-Meier method -Cox Hazards regression -multivariate	Early Referral, age, hemoglobin, Albumin, Cholesterol	ENR>6 months before dialysis was associated with improved survival.

		analysis		
Lorenzo et al. 2004 [60]	Prospective, observational, cohort study in incident dialysis patients (n=538)	-Multivariate Cox analysis -Poisson regression	Age, Albumin	-Patients receive AVF therapy significantly higher versus catheter group -Patients with planned dialysis initiation had higher hospitalization rates and were less likely to initiate dialysis with a catheter
Khan et al 2005 [61]	Retrospective cohort study (1995-1998), analysis patient data from Medicare and Medicaid Service (n=109,321)	-Cox proportional hazard regression	Age, Female, Race, Laboratory, MNC before initiation of dialysis, non-nephrologist visit	-Nephrology care before dialysis is important and consistency of care in the immediate six months before dialysis is a predictor of mortality.
Jungers et al 2006 [62]	Retrospective observational study (1989-2000) of incident dialysis patients (n=1391) in single hospital. (LNR<6 months)	-Cox Proportional model	Age, family factors	-Graded duration of pre-dialysis nephrologist care as a significant independent factor
Schweinger et al 2006 [63]	Retrospective single-center study (n=254) of incident dialysis patients (1998-2001) (LNR<8 weeks)	-Multivariate analysis	Age	-Late referral is more frequent in very elderly -ENR was an independent factor predicting outcome and survival
McClellan WM et al [45]	Respective multi-center study (n=30,327) of ESRD patients 2005-2006. (pre-ESRD >6 months)	-generalized estimating equations (GEE) regression	Race, age, BMI, diabetes, heart failure, atherosclerotic heart disease, peripheral vascular disease and history of amputation, insurance type	-received >= 6 months nephrology care compared with patients who do not received the survival was 85.5% compared with 79.3% -Atherosclerotic Hearth Disease was independently associated with increased pre-dialysis care. -Heart failure, having no health insurance and being unemployed 6 months before start of dialysis, unable to ambulate were associated with decreased care.

NR: Nephrologist referral; ENR: early nephrologist referral; LNR: late nephrologist referral; HR: hazard ratio;

Summary

Although there is still much to be learned about pre-ESRD nephrology care, there is evidence that receiving pre-ESRD nephrology care is associated with lower CKD and ESRD mortality and slower progression. However, factors associated with ESRD vary by many patient and facility level characteristics. To our knowledge, no prior study has examined the facility-level socioeconomic characteristics that may influence pre-ESRD nephrology care and mortality. Adjustment for these relevant factors warrants further investigation.

Medicaid Coverage

Definition

Medicaid is the United States health program for individuals and families with low income and resources. It is a means-tested program that is jointly funded by state and federal government, and is managed by the states. People served by Medicaid are U.S. citizens or legal permanent residents, including low-income adults, their children and people with certain disabilities.[64]

Medicaid Coverage Linked to Socioeconomic Status

Socioeconomic status is a dynamic variable that indicates an individual's social and economic resources [65], which may influence access to healthcare, medical understanding and timeliness of receiving care. The reason SES may influence these may be education, income, medical insurance, social support, and area-based measures based on residence [66], Research has shown that between 1995 and 2004, a social gradient effect was observed between the highest and lowest social classes when separated into quartiles. Those in the lowest SES quartile experienced the highest risk of ESRD, and the risk decreased by improved social class [67].

Several investigators have used insurance status as an indicator for individual SES [68-70], and although the validity of this approach is not known, Medicaid coverage, with the exception of limited medical conditions, is only provided to patients below the federal poverty level 71]. The majority of Medicaid beneficiaries have incomes below the poverty line [72]. Thus, in absence of other SES information, Medicaid coverage is a reasonable surrogate for low SES.

Medicaid Coverage Linked Pre-ESRD Nephrology Care or Early Referral

The association between insurance status and late referral to a nephrologist was examined in two large retrospective studies in the USA. [73-74] According to Kinchen's retrospective cohort study in 81 large dialysis centers, the results revealed that uninsured dialysis patients were three times more likely to be referred late than patients with insurance. [73] As for different insurance coverage type, Winkelmayer et al stated that patients with Medicaid insurance were not at a higher risk to refer late to nephrologist compared to patients with other insurance types.[74] However, Arora et al concluded that patients covered by health care maintenance organizations (HMOs) were referred later than patients covered by Medicaid. [75]. There is currently no literature that evaluates whether patients' Medicaid coverage may be linked to pre-ESRD nephrology care. However, the information gathered on the Medical Evidence form issued by the Centers for Medicare and Medicaid Services showed that Medicaid patients were least likely to have seen a nephrologist before starting renal replacement therapy (RRT). The results was presented by Craig Solid and Allan J Collins of the U.S. Renal Data System (USRDS), noted that Medicare patients and those covered by employer health insurance were 38% and 61% more likely to have seen a nephrologist prior to ESRD onset compared with other members of the study population. Medicaid patients were 15% less likely to receive this care [76].

Summary

In summary, patients who receive Medicaid coverage likely reflect varying socioeconomic status, and there is some evidence that late referral to nephrology varies by patient's socioeconomic status. Even previous studies reported nephrology care before dialysis is important [61] and patient with no insurance [45] have reduced access to care. There exists a gap to evaluate whether patient's insurance coverage effects the association between pre-ESRD care and mortality. Furthermore, compared with previous single-site retrospective study, a multi-center, nationally-representative study is warranted.

Statement of Research Objectives

The purpose of this research project is to assess whether the association between pre-ESRD nephrology care and facility standardized mortality ratio varies based on the proportion of patients with Medicaid coverage in a dialysis facility. The research questions assessed in this work include:

1. What are the trends for facility SMR and the percentage of patient who receive pre-ESRD nephrology care over 4 time periods from 2007 to 2010?
2. Is there an association between the proportion of patients within a facility who received pre-ESRD nephrology care and the facility SMR after adjusted for relevant confounders?
3. If the association exists, does the relationship between pre-ESRD nephrology care and SMR vary based on Medicaid coverage?

CHAPTER 2: MANUSCRIPT

Medicaid Coverage and Pre-ESRD Nephrology Care Influence Patient Mortality among United States Dialysis Facilities

ABSTRACT

Background: Pre-ESRD nephrology care is important for better clinical outcomes for patients with end stage renal disease (ESRD). Timely receipt of nephrologist care was associated with slower chronic kidney disease (CKD) progression, lower rates of adverse outcomes, higher survival, and improved quality life. Delayed care is associated with progression of kidney disease and increased mortality after start of hemodialysis. Prior studies suggest that patient socioeconomic status may be an indicator for late nephrologist referral. The aim of this study was to determine the association between pre-ESRD nephrology care and standardized mortality ratio in dialysis facilities, and to determine whether this association varied by Medicaid health insurance coverage.

Methods: A total of 5,387 dialysis facilities were identified from the Dialysis Facility Report data from 2007-2010, which presented detailed data from the ESRD Medical Evidence Form (FORM CMS-2728) across 18 dialysis facility networks (56 states and territories) in the U.S. Receipt of pre-ESRD nephrology care was based on the CMS 2728 Medical Evidence Form which was completed for all ESRD patients at the time of ESRD start. Standardized mortality ratio (SMR) was calculated as the number of observed deaths within a dialysis facility over the number of expected deaths within a facility. A marginal mixed generalized estimating equation model assuming exchangeable

covariance structure was used to estimate the association between pre-ESRD nephrology care and facility SMR as well as the effect modification of Medicaid coverage.

Results: The percentage of patients who received pre-ESRD nephrology care within a facility was significantly associated with facility-level SMR. In particular, for a ten percent increase in pre-ESRD nephrology care, facility SMR decreased 1.30% (95% CI, 0.90%-1.61%). Compared to facilities whose proportion of patients received Medicaid coverage (MC) greater than the third quartile, facilities whose MC lower than the first quartile experienced a significant 1.10% (95% CI, 0.10%-2.10%) increase in rate of change between pre-ESRD nephrology care and facility SMR.

Conclusion: As the percentage of patients who received pre-ESRD nephrology care within a facility increased, the facility-level SMR decreased. This association was modified by patient Medicaid coverage, where decreased proportion of patients received Medicaid Coverage results in a steeper rate of change. These results suggested that targeted quality improvement interventions to improve access to pre-ESRD nephrology care could reduce mortality among ESRD patients in dialysis facilities.

INTRODUCTION

Pre-ESRD nephrology care from physicians or specialists is important for better clinical outcomes for patients with ESRD [77]. Many studies found that following early nephrology referral, GFR declined more slowly and was associated with better survival. Timely receipt of nephrologist care is associated with slower CKD progression, lower rates of adverse outcomes and improved quality life [78]. Delayed care is associated with progression of kidney disease and increased mortality after start of hemodialysis.

Therefore, U.S. and international practice guidelines recommend that all patients with stage 4 and 5 CKD should be under nephrologist care [79].

Medicaid coverage is a US health care program for certain people and families with low incomes and resources. Medicaid coverage has been used as an indicator for individual socioeconomic status (SES) by several investigators [80-82], and although the validity of this approach is not known, Medicaid coverage, with the exception of limited medical conditions, is only provided to patients below the federal poverty level [83]. The majority of Medicaid beneficiaries have incomes below the poverty line [84]. Thus, in absence of other SES information, Medicaid coverage is a reasonable surrogate for low SES. The association between insurance status, socioeconomic status and late referral to a nephrologist were examined in two large retrospective studies in the USA [67] [45]. According to Kinchen's retrospective cohort study in 81 large dialysis centers, he reported that uninsured dialysis patients were three times more likely to be referred late than patients with insurance [67]. But Winkelmayer et al. stated that patients with Medicaid insurance were at a non-significant higher risk to refer late to nephrologist compared with other insurance types [45].

Because of previous inconsistent results, our research evaluates whether patient's Medicaid coverage would affect the association between pre-ESRD nephrology care and mortality. Differences between patients receive Medicaid coverage are possible factors that might contribute to variation in pre-ESRD nephrology care. If clinically relevant Medicaid coverage variation in pre-ESRD nephrology care exists, then health policies might be designed to reduce the risk for delayed or absent care.

METHODS

Study Population

The Dialysis Facility Report dataset is created annually under a contract to the Centers for Medicare & Medicaid Services (CMS) to provide dialysis facilities, patients, state surveyors, and regions with valuable information on patient characteristics, treatment patterns, hospitalization, mortality, and transplantation patterns in their facilities. This study used Dialysis Facility Report (DFR) data from 2011, which included detailed characteristics of new patients in each facility by year from the ESRD Medical Evidence Form (FORM CMS-2728). Hemodialysis and peritoneal dialysis patients who started dialysis between January 1, 2007 and December 31, 2010 were included. The University of Michigan Kidney Epidemiology and Cost Center produced this nation-wide report of 5,387 dialysis facilities across 18 networks (56 states and territories) in the US.

Pre-ESRD Nephrology Care Coverage

The primary exposure of interest was receipt of nephrology care prior to ESRD. Receipt of pre-ESRD nephrology care was based on the CMS 2728 Medical Evidence Form which was completed for all ESRD patients at the time of ESRD. We defined the proportion of patients who received pre-ESRD nephrology care within a facility as the difference between 100 and the percentage of patients with no access to pre-ESRD in 2007, 2008, 2009, and 2010.

Standardized Mortality Ratio (SMR)

The primary outcome of interest for this study was the standardized mortality ratio (SMR). The SMR is calculated as the number of observed deaths within a dialysis facility over the number of expected deaths within a facility. The expected death rate was calculated based on the national death rate in the same year by adjusting for calendar year, age, race, ethnicity, sex, diabetes, duration of ESRD, nursing home status, comorbidities at incidence, BMI at incidence, state, and population death rates. SMR was analyzed as a continuous variable. In order to avoid skewness and reduce the effect of outliers, logarithmic transformation of SMR was used for further analysis.

Medicaid Coverage

The non-modifiable adjusted risk factor was percentage of patients who received Medicaid coverage only within each facility in 2007, 2008, 2009 and 2010.

Other Facility and Clinical Characteristics

The standardized mortality ratio has already been adjusted for many patient-level characteristics, therefore, only percentage smokers, percentage of patients with arteriovenous fistula (AV) present and percentage of erythropoietin-stimulating agent (ESA) use prior to dialysis, the number of patients, the number of total staff position on December 31th, and facility profit status (profit vs. non-profit) were included for further regression analysis.

Statistical Analysis

Means and standard deviations (SD) were calculated for all continuous variables.

To compare the changes in SMR, pre-ESRD nephrology care and other relevant covariates over 4 year time period were considered repeated measurements and were modeled assuming an exchangeable covariance structure using generalized estimating equations.

We obtained a crude estimate of the association between pre-ESRD nephrology care and SMR using linear regression, controlling for clustering within dialysis facilities using generalized estimating equations. Variables considered as potential confounders were selected based on prior literature documenting risk factors for dialysis facility mortality or association with nephrology care. We then conducted bivariate analysis with the outcome and then with the exposure to identify potential confounders in our dataset. Because SMR has already been adjusted for many variables, we only performed these analyses for variables not already adjusted for SMR.

The full model that included all potential confounders was then developed. We used the 10% guideline to assess confounding by precision and the Wald test to test for the significance of effect modification. The SAS GENMOD procedure was used to perform all analyses and produced clustered robust SEs that corrected for within-facility correlation. In order to completely estimate the non-modifiable effect modifier of percentage of patients who received Medicaid coverage only, we stratified Medicaid coverage into quartiles.

In order to evaluate different classifications of pre-ESRD nephrology care, we repeated the main analysis by re-defining our primary exposure pre-ESRD nephrology care by the

percentage of patients who received pre-ESRD nephrology care greater than 12 months vs. greater than 6 months.

All of the analyses were performed using SAS 9.3 (SAS institute, Cary, NC) and p-values were considered statistically significant at an alpha level of 0.05.

RESULTS

Baseline Year Study Population

At baseline year 2007, the majority facilities were profit facilities (83.24%) and larger proportion of patients were no access to pre-ESRD nephrologist care (30.64%). As for other relevant covariates, older age (63.02), high percent of white patients (66.43%), slightly higher proportion of Medicare and Medicaid coverage only patients (19.71%) and high prevalence of congestive heart failure (32.17%) were major characteristics in baseline year across 5,387 dialysis facilities. (Table 1)

Longitudinal Change in Standardized Mortality Ratio, pre-ESRD Nephrologist Care and Relevant Covariates

Overall, the mean SMR from 2007 to 2010 was 1.03, 1.02, 1.03, 1.03 respectively, and there was no significant rate of change in SMR over 4 years. For the primary exposure variable, the mean percentage of patients with pre-ESRD nephrologist care from 2007 to 2010 was 69.36%, 70.09%, 70.05%, and 69.89% respectively, and there was no significant rate of change over 4 years' time period. For other relevant covariates, the mean level of percentage ESA use ($P<0.0001$) declined over 4 years follow-up with -2.35% rate of change. There was an increased percentage of patients with Medicaid

coverage only (P<0.0001) over time, with a 0.27 rate of change. Similarly, there was an increase in the percentage of patients with an AV fistula present (P<0.0001) with a 0.57% rate of change. Other relevant covariates revealed no significant change over the 4-year study time frame (Table 2)

Association between Potential Covariates and Pre-ESRD Nephrologist Care and Standardized Mortality Ratio

There were no significant associations between facility-level characteristics (number of patients per facility, number of staff per facility and percent of facility for profit) and pre-ESRD nephrologist care, but all were associated with the SMR. For patient characteristics within a facility, all four relevant covariates (percent of patients with insurance, percent of patients who were current smokers, percent of patients with an AV fistula, and percent of patients with ESA prior to dialysis) were significantly associated with pre-ESRD nephrologist care and the SMR (Table 3).

Association between Pre-ESRD Nephrology Care and Standardized Mortality Ratio

There was a crude decreased rate of change between the percentage of patients receiving pre-ESRD nephrology care and SMR within a dialysis facility. For a ten-percent increase in pre-ESRD nephrology care, the SMR decreased 1.30% (95% CI, 0.90%-1.61%). When we further adjusted for confounders, the association between pre-ESRD nephrology care and SMR was attenuated but still significant. For a ten-percent increase in pre-ESRD nephrology care, SMR decreased 0.50% (95% CI, 0.10%-0.80%). In order to evaluate the effect modification of covariates on the primary exposure pre-ESRD nephrology care, we analyzed the marginal model by adding seven interaction terms. The association between

pre-ESRD nephrology care and SMR was not modified by all of the adjusted covariates (Table 4).

Association between Pre-ESRD Nephrology Care and Standardized Mortality Ratio Modified by Percentage of Patients Receiving Medicaid Coverage Only

To more completely evaluate the effect modification by Medicaid health insurance coverage status, we stratified facilities by 4-year mean percentage of patients receiving Medicaid Coverage only (MC) based on quartiles (MC≤5.89, 5.89<MC≤14.09, MC>14.09). Compared with the group whose MC was among the highest quartile, the group whose MC was between the first and third quartile had a 0.2% (95% CI, -0.50%-0.90%) increase in rate of change between pre-ESRD and SMR and this association was not statistically significant. However, the association between pre-ESRD nephrology care and SMR was steeper among facilities with a lower proportion of patients on Medicaid coverage. Compared with facility group whose MC was in the highest quartile, the group whose MC was in the lowest quartile had a 1.10% (95% CI, 0.10%-2.10%) increase in the rate of change between pre-ESRD and SMR after controlling for other relevant confounders (P for interaction=0.0157) (Table 5).

Sensitivity Analysis

After re-defining pre-ESRD nephrology care as the proportion of patients who received pre-ESRD nephrology care greater than 6 months, the association between pre-ESRD nephrology and facility SMR was more significant, where a ten percent increase in the percentage of patients who received pre-ESRD nephrology care within a dialysis facility, there was a 0.70% (95% CI, 0.10%-1.20%) decrease in facility SMR. There was no

significant interaction by the percentage of patients who received Medicaid coverage on this association. Even after further stratification of Medicaid coverage by first and third quartiles (MC≤5.89, 5.89<MC≤14.09, MC>14.09), the interaction term was not significant (Table 5).

When pre-ESRD nephrology care was examined as the proportion of patients who received pre-ESRD nephrology care more than 12 months, the association showed that a ten percent increase in the percentage of patients who received pre-ESRD nephrology care within a dialysis facility resulted in a 1.00% (95% CI, 0.60%-1.50%) decrease in facility SMR. Patient Medicaid coverage was not an effect modifier on this association. However, when stratified patient Medicaid coverage by quartile (MC≤5.89, 5.89 < MC≤14.09, MC>14.09), this association was statistically significantly different between facilities whose MC≤5.89 and MC>14.09. Compared with facilities whose MC>14.09, the facilities whose MC≤5.89 experienced a 1.0% (95% CI, 0.20%-1.80%) increase in rate of change between pre-ESRD nephrology care and facility SMR (Table 5).

DISCUSSION

Most research on pre-ESRD care among patients with ESRD has only focused on the timing of nephrology care and other patient level characteristics, but the role of SES has only recently received attention. One recent study reported that community poverty is associated with decreased likelihood of AVF use [85]. Another study found that late nephrology referral was associated with lower social economic status (indicated by enrollment in Medicaid or other state program for the poor) [86]. To our knowledge, our study is the first to examine whether the association between pre-ESRD nephrology care

and facility SMR is modified by Medicaid coverage using nationally-representative data on the dialysis facility level. Because pre-ESRD care may influence late-stage CKD and ESRD survival, an examination of this important indicator of access to care is an important step toward a more public health-oriented understanding of late CKD and ESRD care. In this study, several significant findings have important clinical and public policy implications.

Our most important finding was that as the proportion of patients who received pre-ESRD nephrology care increases, the facility SMR decreases. Furthermore, this association was modified by the percentage of patients who received Medicaid coverage only. Facilities within the lowest quartile of Medicaid coverage experienced a 1.10% increase in the rate of change between pre-ESRD nephrology care and facility SMR compared with facilities within the highest quartile of Medicaid coverage after adjustment for relevant confounders. Although the association between high proportion of pre-ESRD nephrology care and decreased risk for mortality has been extensively reported, the nature of the Medicaid coverage on the relationship has not, and recognition of this variability may be relevant in efforts to improve late-stage CKD care.

The reason for this significant difference was likely related to timing of pre-ESRD nephrology care. A dialysis facility that has a higher proportion of patients with Medicaid insurance coverage suggests these patients have a lower socioeconomic status, which may also relate to high prevalence of late referral. Late referral has often been defined as referral of a patient with progressive kidney failure to a nephrologist less than 3 months before the need to start dialysis, but definitions of late referral vary largely and time limits ranging between immediate dialysis and <6 months have been used. Factors that

might influence this timing difference include characteristics of the (1) antecedent kidney disease, (2) patient, (3) physician, and (4) health care system-related reasons. [87] Disease-related factors that might account for variations in pre-ESRD nephrology care include the prevalence of undetected, asymptomatic CKD in a population, and 15 to 20% of all incident ESRD patients may fall into this pattern of CKD progression. Although we are unable to examine CKD stages in our study, the median time spent in stage 3 CKD before ESRD is reported to be >2.5 yr. and that in stage 4 CKD >2 yr. This suggests that there is ample time before ESRD for detection of CKD and nephrology referral.

Patient-related factors might account for the facility-level variations in pre-ESRD care that we observed. Yan et al. found that the distance to the center might be a potential reason for late referral for ESRD patients. It appears that patients with low SES may live in isolated rural areas with no nephrologist nearby and may need to travel long distances in order to see a specialist. There is often no public transportation in these areas, further contributing to the increased likelihood of delays in receiving specialist care. Furthermore, Cass et al. stated within the same Australian region, patients living within a low socioeconomic status area were more often referred late to nephrology care.

Physician-related factors may also influence access to early nephrology care. Causes related to the primary care physician (PCP) and/or the nephrologist certainly explain a large proportion of late referral pattern. Kidney diseases are infrequent and complex; therefore, it is different for each PCP to accumulate enough clinical experience for optimal follow-up of those patients. Variability exists across geography and poverty status. This is supported by the recent Agency for Healthcare Research and Quality report documenting that rural residents are less likely than their urban counterparts to receive

recommended preventive services and made fewer visits to health care providers. It is likely that between different facilities, PCP's experience and whether nephrologist sufficient time devoting to the patient at the right moment could explain some of the rate of change between pre-ESRD nephrology care and SMR variation.

Finally, health care system-related factors also could attribute to this variation. Even in Western countries, some patients with poor SES may have no or only limited access to care. Some health care plans restrict referral to specialized care or consults. Regulated or deregulated reimbursement of drugs such as prescription or delivery of ESAs, biological and radiological investigations may also play a role in the association between Medicaid coverage, pre-ESRD nephrology care, and mortality.

A novel aspect of this study was the evaluation of effect modification of Medicaid coverage within a facility on pre-ESRD nephrology care and facility SMR. To our knowledge, this study is the first to document this relationship within a nationally representative population of US dialysis facilities. Another novel aspect of this study was that we evaluated both facility- and patient-level characteristics. Prior studies have been limited by little patient follow-up result.

The limitations of this study beyond those already discussed should be noted. The pre-ESRD care data derived from CMS 2728 forms are subject to misclassification, have not been validated, and may be centered differentially by poorly performing treatment centers. The strong association between reported pre-ESRD care and facility standardized mortality ratio and that the system uniformly collects mortality data suggest that it is unlikely that individuals lost to follow-up contributed to any substantial selection bias.

The DFR data are based upon CMS 2728 surveillance data, which have virtually 100% follow-up. An additional limitation is that residual confounding persists; we were unable to control for all possible confounders of the association between pre-ESRD nephrology care and SMR.

In conclusion, we found that as the percentage of patients who receive pre-ESRD nephrology care within a facility increases, facility SMR is lower. Further, this association is modified by patient Medicaid coverage, where the effect of pre-ESRD nephrology care on mortality was stronger among facilities that had a lower proportion of patients on Medicaid insurance. This suggests that targeted quality improvement interventions to improve access to pre-ESRD nephrology care might be warranted in these populations to reduce mortality in ESRD patients. Furthermore, perhaps increasing patient access to health care insurance other than Medicaid may further reduce facility-level SMR.

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Table 1. Baseline Demographic and Clinical Characteristics of Dialysis Facilities within the Study Population (N=5,387)

	Mean (SD) or n (%)
Facility Characteristics	
Number of Patients per facility	110 (69)
Number of Staff	15 (9)
% For Profit	4489 (83.24%)
Patient Characteristics within Facilities	
Primary Exposure	
Pre-ESRD nephrologist Care (%)	
Pre-ESRD Nephrologist Care Less than 6 months	11.33 (16.428)
Pre-ESRD Nephrologist Care Between 6 and 12 months	23.23 (18.545)
Pre-ESRD Nephrologist Care More Than 12 months	23.38 (19.796)
No Access to Pre-ESRD Nephrologist Care	30.64 (20.838)
Other Relevant Covariates	
Age (year)	63.02 (7.640)
Female (%)	44.43 (15.841)
Race (%)	
African American	28.31 (29.186)
Asian/Pacific Islander	3.34 (9.397)
White	66.43 (29.629)
Hispanic	11.71 (21.100)
Insurance Status (%)	
Employer group health insurance	16.44 (14.443)
Medicaid coverage only	10.99 (12.051)
Medicare coverage only	19.71 (15.167)
Medicare and Medicaid coverage only	12.64 (12.66)
No insurance	7.07 (10.014)
Other Insurance	8.01 (12.007)

Table 1 (continued): Baseline Demographic and Clinical Characteristics of Dialysis Facilities in the Study Population (N=5,387)

Body mass index	
Median BMI for males >=20 years	27.32 (3.280)
Median BMI for female >=20 years	28.81 (4.367)
Diabetes (%)	57.65 (17.204)
Current Smoker (%)	6.72 (8.910)
AV Fistula Present (%)	13.81 (12.982)
% ESA Prior to Dialysis	28.72 (21.224)
Comorbid conditions	
Chronic Obstructive Pulmonary Disease (%)	9.05 (10.340)
Congestive Heart Failure (%)	32.17 (18.721)
Peripheral Vascular Disease (%)	14.33 (14.710)
Atherosclerotic heart Disease (%)	21.18 (19.917)
Cancer (%)	7.29 (8.948)
Number of Comorbidities	3.06 (0.873)

Table 2. Longitudinal Change in Standardized Mortality Ratio, pre-ESRD Nephrologist Care and Relevant Covariates among Dialysis Facilities in the Study Population

	Rate of Change from 2007 to 2010	P value
Facility Characteristics		
Number of Patients per facility	1.2167	<0.0001
Number of Staff	0.09674	0.0061
Patient Characteristics within Facilities		
Primary Exposure		
Pre-ESRD nephrologist Care (%)	0.1265	0.2488
Outcome		
Standardized Mortality Ratio	0.002852	0.2059
Other Relevant Covariates		
Insurance (%)	-0.1358	0.0131
Current Smoker (%)	0.03854	0.4640
AV Fistula Present (%)	0.5546	<0.0001
ESA Prior to Dialysis (%)	-2.3154	<0.0001

Table 3. Association between Potential Covariates and Pre-ESRD Nephrologist Care and Standardized Mortality Ratio among US Dialysis Facilities

	Primary Exposure		Outcome	
	Pre-ESRD Nephrologist Care		Standardized Mortality Ratio	
	Rate of Change	P value	Rate of Change	P value
Facility Characteristics				
Number of Patients per facility	-0.00018	0.9844	0.0002	0.0023
Number of Staff	-0.0103	0.6686	-0.0013	0.0005
% For Profit	-0.1362	0.8379	-0.1020	<0.0001
Other Relevant Covariates				
Medicaid Coverage only (%)	-0.1222	<0.0001	0.0009	0.0022
Current Smoker (%)	-0.0675	0.0042	-0.0010	0.0045
AV Fistula Present (%)	0.3918	<0.0001	-0.0036	<0.0001
ESA Prior to Dialysis (%)	0.2547	<0.0001	-0.0022	<0.0001

Table 4. Association between Pre-ESRD Nephrologist Care and Log-transformed Standardized Mortality Ratio

	Unadjusted Model			Adjusted Model		
	Estimate	**Standard Error**	**P-value**	**Estimate**	**Standard Error**	**P-value**
Primary Exposure						
Pre-ESRD Nephrologist Care	-0.00108	0.000147	<0.0001	-0.00051	0.000150	0.0006
Non-Modifiable Adjusted Risk Factor						
Patient Received Medicaid Coverage only (%)				0.00012	0.00030	0.6832
Adjusted Potential Confounders						
For Profit or not				-0.08179	0.000374	<0.0001
# patients in a facility				0.00377	0.01018	<0.0001
# of staff in a facility				-0.00182	0.00060	0.0056
Current Smoker (%)				-0.00253	0.00030	<0.0001
AV Fistula Present (%)				-0.00477	0.000374	<0.0001
ESA Prior to Dialysis (%)				-0.00164	0.000229	<0.0001

Table 5: Association between Pre-ESRD Nephrologist Care and Standardized Mortality Ratio (SMR), Stratified by Quartile of Patient Medicaid Coverage (MC)

	Association between Pre-ESRD Nephrology Care and SMR		
Pre-ESRD Definition	**Smaller than First Quartile MC≤5.89**	**First Quartile to Third Quartile 5.89<MC≤14.09**	**Greater than Third Quartile MC>14.09**
Pre-ESRD>0 Month	**Reference Group**	0.20% (95% CI, -0.50%-0.90%)	1.10% (95% CI, 0.10%-2.10%)
Pre-ESRD≥6 Months	**Reference Group**	0.21% (95% CI, -0.49%-0.89%)	0.52% (95% CI, -0.15%-1.10%)
Pre-ESRD≥12 Months	**Reference Group**	0.33% (95% CI, -0.20%-0.79%)	1.00% (95% CI, 0.20%-1.80%)

CHAPTER 3: SUMMARY, PUBLIC HEALTH IMPLICATION, POSSIBLE FUTURE DIRECTION

SUMMARY

In summary, our study found that there was a significant decreased association between the proportion of patients who received pre-ESRD nephrology care and the dialysis facility-level standardized mortality ratio. Furthermore, this association was modified by the percentage of patients who received Medicaid coverage only. Facilities within the lowest quartile of Medicaid coverage experienced a 1.10% (95% CI, 0.10%-2.10%) increase in the rate of change between pre-ESRD nephrology care and facility SMR compared with facilities within the highest quartile of Medicaid coverage after adjustment for relevant confounders. Moreover, when we examined the timing of pre-ESRD nephrology care by greater than 6 months, this association was stronger in that a ten percent increase of patients who receive pre-ESRD nephrology care with in a dialysis facility resulted in a 0.70% (95% CI, 0.10%-1.20%) decrease in facility SMR. When we examined the timing of pre-ESRD nephrology care as greater than 12 months, a 10% increase in the proportion of patients who received pre-ESRD nephrology care within a dialysis facility resulted in a 1.00% (95% CI, 0.60%-1.50%) decrease in facility SMR. Medicaid coverage was still an effect modifier in those two situations.

Based on our analysis, pre-ESRD nephrology care was associated with facility SMR. A higher proportion of patients who received pre-ESRD nephrology care within a facility were associated with a better clinical prognosis as indicated by the facility standardized mortality ratio. Also, patient Medicaid coverage modified this association, which suggests that patient socioeconomic status could explain some variation in pre-ESRD nephrology care.

PUBLIC HEALTH IMPLICATION

Our study results support the evidence that pre-ESRD nephrology care from physicians or specialists is important for better clinical outcomes for patients with ESRD. With an increasing prevalence of patients undergoing maintenance dialysis in the United States, renal disease guidelines should strengthen their recommendations and requirements to ensure that all patients with stage 4 and 5 CKD receive nephrologist care prior to progressing to ESRD. Furthermore, the percentage of patients who receive pre-ESRD nephrology care within a facility did increase over the 4-year time period, but this was not a statistically significant increase. This suggests that perhaps more effective regulations for pre-ESRD nephrology care be implemented across US dialysis facilities. Patient Medicaid coverage was an effect modifier on the association between pre-ESRD nephrology care and facility standardized mortality ratio. This suggests that pre-ESRD nephrology care and low socioeconomic status influence mortality among patients within US dialysis facilities.

POSSIBLE FUTURE DIRECTION

While considering the limitation and difficulties within this work, it is important to recognize the need for continued analyses. As this thesis focused on the association between the percentage of patient receive pre-ESRD nephrology care and facility standardized mortality ratio, and whether this association was modified by patient Medicaid coverage. There were only a few previous studies that reported that race and distance between home and facility could explain some variation for nephrology late referral. Those factors could also explain some variation for our study results, so future

study could focus on these topics. With these later analyses, it will be informative to see the possible reason for this effect modification and new recommendations can be provided to help low socioeconomic status patient overcome those barriers. These recommendations serve as tools for policy makers as they continue to develop ways to delay the progression of ESRD.

The definition of pre-ESRD nephrology care is ranges between immediate dialysis and >12 months. As this thesis only compared different results by varying timing pre-ESRD nephrology care definition based on facility level data records, future work should develop higher power study such as case-control study to support and validate these time points. If these variations exist, health policies should develop clear guidelines and recommendations for how to define pre-ESRD nephrology care and standardize how and when patients should receive this care.

When comparing facility level data, longitudinal models, such as the models developed in this project, have a distinct advantage in being able account for within-facility correlation. When analyzing longitudinal models it is important to recognize and account for correlation of repeated measures on one subject in order to make correct inference. The mixed marginal model developed in this paper allowed for specific covariance structure within each cluster over the four-year time period. Future development of these mathematical models may better account for both between and within subject's variations and could help to draw subject-specific conclusions.

Missing information is inevitable in longitudinal studies, and can results in biased estimates and a loss of power. In this thesis, we have almost 10% missing outcome

observations for the whole population and even though statistical software could automatically account for missing values, we still expect mathematical methods to deal with those missing values. Previous studies have already developed several methods such as instead missing value as population mean, previous row mean, or mean of observations before and after values or even regression based method. Future development of these methods may warrant more precise results. However, this study offers an important first step in our understanding of the role of pre-ESRD nephrology care, access to health insurance, and mortality among ESRD patients receiving care in US dialysis facilities.