IMPACT OF AUTOMATIC REPORTING OF ESTIMATED GLOMERULAR FILTRATION ON CHRONIC KIDNEY DISEASE DETECTION AND PATIENT CARE IN A HOSPITAL SETTING

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A dissertation submitted to the faculty of the University of North Carolina at Chapel Hill in partial fulfillment of the degree of Doctor of Philosophy in the Department of Epidemiology in the Gillings School of Global Public Health.

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ABSTRACT

Monique Ahinee Amamoo: Impact of Automatic Reporting of Estimated Glomerular Filtration on Chronic Kidney Disease Detection and Patient Care in a Hospital Setting (Under the direction of Gerardo Heiss)

BACKGROUND AND OBJECTIVES

In an attempt to address rising concerns about low and delayed detection of chronic kidney disease (CKD) several healthcare organizations and clinical laboratories developed initiatives to automatically report estimated glomerular filtration rates (eGFR) in response to the National Kidney Foundation-Kidney Disease Outcome Quality Initiative (KDOQI) clinical recommendations. In April 2005 the University of North Carolina at Chapel Hill Healthcare System (UNCHS), introduced an eGFR reporting initiative to facilitate monitoring of CKD in its patient population. This initiative automatically reports eGFR levels calculated using the Modification of Diet in Renal Disease (MDRD) equation on all serum *creatinine* tests ordered for adults 18 and older. This doctoral dissertation examined the impact of the UNCHS eGFR reporting initiative on CKD detection and nephrology appointments.

DESIGN, SETTING, PARTICIPANTS, & MEASUREMENTS

This study used administrative billing and electronic medical record data from adult patients who sought care in the University of North Carolina at Chapel Hill Healthcare System from 2004-2010 and had at least one serum creatinine measurement. Patient demographics, CKD diagnosis, comorbidities, and laboratory results were retrieved from medical records. Billing data was used to determine nephrology scheduling status. Measures

of CKD detection and nephrology appointments were compared for the 15 months prior, and the 48 months following the introduction of the initiative to automatically report eGFR.

RESULTS

An increase of 9% in the overall detection of CKD within the UNC healthcare system was observed following the introduction of the eGFR reporting initiative. Those with moderate CKD, older age, male gender, white race and CKD risk factors had higher detection rates during the period following the introduction of the eGFR reporting initiative, but no detectable differences in scheduled nephrology appointments were observed following the UNCHS eGFR reporting initiative. Those with diagnoses of hypertension, diabetes and cardiovascular disease had lower odds of having a nephrology appointment scheduled, irrespective of eGFR reporting period.

CONCLUSIONS

Introduction of automated eGFR reporting was followed by a moderate increase in CKD detection. eGFR reporting had no discernible association with scheduling of nephrology appointments within UNCHS.

I dedicate this dissertation research to the memory of Big Mama, Mama Grace, Granddaddy Charles, Granddaddy James, Auntie Ahinee and Peepaw

To Micah Mawuena Mortey, Mykelti, and my nieces and nephews, know that all things are possible through Jesus Christ who gives you strength and as long as you place God first in all you do, you will be successful.

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"Now all glory to God, who is able, through his mighty power at work within us, to accomplish infinitely more than we might ask or think. Glory to him in the church and in Christ Jesus through all generations forever and ever! Amen". Ephesians 3:20-21

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LIST OF ABBREVIATIONS

CDW-H- Clinical Data Warehouse

CI- Confidence Interval

CIR- Cumulative Incidence of Detection rate

CKD- Chronic Kidney Disease

CVD- Cardiovascular Disease

eGFR- Estimated Glomerular Filtration Rate

EHR- Electronic Health Record

ESKD- End-Stage Kidney Disease

GFR- Glomerular Filtration Rate

ICD-9- CM International Classification of Diseases (version 9)- Clinical Modification

ICD-9 International Classification of Diseases (version 9)

KDOQI- Kidney Disease Outcomes Quality Initiative

MDRD- Modification of Diet in Renal Disease

NCTRaCS- North Carolina Translational Science Institute

NHANES- National Health and Nutrition Examination Survey

NIH- National Institutes of Health

NKF- National Kidney Foundation

NKF-KDOQI- National Kidney Foundation- Kidney Disease Outcomes Quality Initiative

OR- Odds ratio

SCr- Serum Creatinine

SES- Socio-economic status

UNC P&A- University of North Carolina at Chapel Hill Physicians and Associates

UNC- University of North Carolina at Chapel Hill

UNCHS- University of Chapel Hill Healthcare system

WebCIS- WebClinical Information Systems

CHAPTER ONE: BACKGROUND AND SIGNIFICANCE

The Epidemiology of Chronic Kidney Disease

Chronic Kidney Disease (CKD) is an escalating public health issue affecting one in ten Americans with another 20 million at risk. In 2007, approximately 26.3 million Americans were living with CKD (Stages 1-4), representing 13.1 % of the US non-institutionalized adult population.[1]

The Burden of CKD is progressively increasing. The prevalence of CKD has increased from 10.1% in 1988-1994 to 14.0% in 2005-2010.[1, 2] The number of individuals with Stage 5 CKD also referred to as end-stage kidney disease (ESKD), has increased dramatically from 14,500 in 1978 to 527,283 in 2007 and 593,086 in 2010.[2-4]

CKD has been associated with demographic factors. Age is associated with an increased prevalence of CKD.[5-9] Among participants in the National Health and Nutrition Examination Survey (NHANES) (2005-2010), the prevalence of CKD increased with age and was highest among those 60 years and older (35.0%)[2]. CKD prevalence is also higher among women compared with men (15.8% vs. 12.1%) and African Americans compared with Whites (16.0% vs. 14.3%) [2, 6, 8-13] In NHANES 1999-2000, the prevalence of CKD was 26% higher among women compared to men and varied by race-ethnicity for Whites (4.2%), African-Americans (3.4%), and Mexican-Americans (1.2%) [8].

Low socio-economic status (SES) and life-course SES are also associated with CKD.[14-19] Less than a high school education was associated with an increased odds of CKD for both African-Americans and Whites compared with those with a college degree in the Atherosclerosis Risk in Communities Study (OR=1.6, 95% CI (1.1, 2.5) for African-Americans; OR=1.75, 95% CI (1.2, 2.5) for Whites)[18]. An investigation of life -course socioeconomic status revealed, the odds of CKD among middle-aged participants who reported working when 30 years old were higher than those participants who reported being unemployed when they were 30 years old (OR=1.4; 95% CI (1.0, 2.0) for Whites; OR=1.9, 95% CI (1.2, 3.0) for African-Americans)[18].

Burden of Chronic Kidney Disease

CKD causes premature morbidity and mortality. CKD is associated with 2-3 fold increase in the risk of all-cause mortality.[8] Patients with CKD are at increased risk for complications from infections, strokes, and premature cardiovascular diseases.[3, 8] Additionally, those with CKD are hospitalized at higher rates than those without CKD, even after adjusting for prior hospitalizations, comorbidities and sex.[3]

Kidney disease has a substantial impact on the health care system. CKD patients, compared to -age-matched patients without CKD, experience more health care costs, physician visits, prescriptions, and are twice as likely to be hospitalized.[20] The costs of delivering care to ESKD patients in 1999 was estimated at 17.9 billion dollars, 13% higher than the total National Institutes of Health (NIH) budget for the year[21]. The total Medicare expenditures for ESKD care in 2010 rose by 8.01% to $32 billion, which represented 6 % of the total Medicare

budget[2]. Healthcare costs associated with CKD and ESKD are increasing. In 2006 the healthcare costs for CKD patients with Medicare were $49 billion, nearly 5 times the costs of care in 1993. Similarly, the healthcare cost for those with an Employer Health Group Plan in 2006 was 11 times greater, at $1.2 billion, than the costs in 2000 [22].

Detection and Treatment of Chronic Kidney Disease

CKD is asymptomatic, and when left untreated can progress to complete kidney failure or end-stage kidney disease (ESKD). ESKD is a chronic disease for which the only treatments are dialysis and transplantation. The incidence of ESKD has doubled every year since 1980, and an estimated 385,200 people in the U.S. currently live with ESKD. By 2030, the estimated number of new cases of ESKD will exceed 450,000, and over 2 million people will be on dialysis [23]. CKD and ESKD lower patient quality of life, cause premature morbidity and mortality, and cause economic burden on individuals, health care systems and society.[20] However, if chronic kidney disease is detected early, treatments can be successful in slowing the progression to kidney failure.[24-27]

Clinical Practices to Detect Chronic Kidney Disease

For years clinical practices used serum creatinine (SCr) levels as a surrogate marker for kidney filtration because of the ease and cost effectiveness of this measurement. Due to the limitations of SCr to adequately measure kidney function, estimating glomerular filtration rate (eGFR) equations were developed. National Kidney Foundation (NKF) clinical recommendations[28] support the use of the abbreviated Modification of Diet in Renal Disease Study (MDRD) equation to help facilitate an easier mechanism for estimating GFR.[29]

$$GFR=186* [SCr]^{-1.154} *[Age]^{-0.203} *[0.742 \text{ if female}]*[1.212 \text{ if black}].$$

Physicians manually estimate kidney function using the MDRD equation and use the current established National Kidney Foundation- Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) workgroup clinical guidelines[28] for defining the stages of CKD.

Table 1- Stages of Chronic Kidney Disease

Stage	Description	GFR (mL/min/1.73m^2)
1	Kidney damage* with normal or ↑ GFR	≥90
2	Kidney damage* with normal or ↓ GFR	60-89
3	Moderate ↓ GFR	30-59
4	Severe ↓ GFR	15-29
5	Kidney failure	<15 (or dialysis)

*Kidney damage is defined as any structural or functional abnormalities of the kidney detected by pathological abnormalities or by the presence of sediments, blood, or proteinuria in the urine[30].

Automatic eGFR reporting facilitates earlier detection. In 1999, The National Kidney Foundation- Kidney Disease Outcome Quality Initiative (KDOQI) developed guidelines to identify and manage kidney disease at earlier stages.[28] The KDOQI guidelines recommended that all laboratories automatically report eGFR, calculated using the MDRD equation, whenever serum creatinine (SCr) is measured. The implementation of this automatic reporting eliminates the need for physicians to manually determine eGFR and helps facilitate the early detection of CKD.

Currently, eight US states (Connecticut, New Jersey, New York, Louisiana, Michigan, Pennsylvania, Tennessee, and Texas)[31] and several healthcare agencies have passed state

policies requiring automatic eGFR reporting. Many international and US-based healthcare organizations and laboratories implemented policies that would automatically report eGFR when SCr is measured [31-35]. Although the utility and role of automatic eGFR reporting remains unsettled, studies have shown that eGFR reporting resulted in increased CKD detection, referrals, consults, and first time visits to nephrology clinics [34, 36-40].

Based upon recommendations from the North Carolina Institute of Medicine Task Force on Chronic Kidney Disease[41], the University of North Carolina at Chapel Hill Healthcare system (UNCHS), voluntarily implemented automatic eGFR reporting in April 2005. UNCHS implemented a system-wide CKD initiative to automatically report eGFR (based on the MDRD equation), on all SCr tests ordered on adults 18 years or older. Along with this voluntary mandate, the UNCHS collaborated with the UNC Kidney Center to develop education programs for health professionals and the general population, to increase CKD awareness among healthcare providers and improve detection.

Early Detection and Intervention Can Reduce Burden of Disease

Patients referred earlier to nephrologists have fewer CKD complications and lower mortality rates, than those who are referred late.[42] The 5-year survival rate for ESKD is 2 times as high for those who are referred to nephrologists early, at least 6 months prior to dialysis, compared to those referred late, (less than 6 months prior to dialysis), 72.4% vs. 35.2%, respectively[43]. Nephrology referrals in the early disease stages reduce the likelihood that patients will require emergency dialysis, and increase the likelihood of receiving standard renal therapy or pre-dialysis transplantations [44, 45]. Once CKD is detected, kidney protective

treatments can be successful in slowing the progression to kidney failure and facilitating the optimal management of co-morbid conditions.[24-27]

Despite knowledge that early detection is the key to slowing the progression of kidney disease, many patients are getting delayed referrals to nephrologists. Studies have documented primary care physician referrals to nephrologists range from 15 to 83%.[46] Late referrals to nephrologists have resulted in higher hospitalization rates, late initiation of dialysis, higher mortality rates, increased incidence of anemia, bone disease and other CKD complications [47-50]. Approximately 20-35% of those starting dialysis are due to late referrals. However, if patients are referred earlier to nephrologists CKD complications and mortality rates can be reduced.[42]

Screening for CKD is necessary for identifying early CKD patients and ensuring timely referral to nephrologists. In 1999, The National Kidney Foundation- Kidney Disease Outcome Quality Initiative (KDOQI) developed guidelines to identify and manage kidney disease. The KDOQI guidelines recommend that all physicians assess clinical and socio demographic factors associated with kidney disease such as family history of kidney disease, older age, smoking, low birth weight, hypertension or diabetes during each patient's health care visit. If any of these factors are identified in the patients, then kidney function, through an assessment of albuminuria and GFR should be estimated to screen for chronic kidney disease. Within the KDOQI guidelines, recommendations were made to increase the CKD screening practices within health care systems. However, health care systems have failed to provide regular

CKD screenings for patients.[46] Lack of awareness and policy mandates could be barriers to detecting and preventing kidney disease.

CHAPTER TWO: SPECIFIC AIMS AND RATIONALE

Chronic kidney disease (CKD) is a growing public health concern affecting more than 26 million Americans [10]. CKD is often asymptomatic and, if untreated, may progress to end-stage kidney disease (ESKD) requiring dialysis therapy and organ transplantation. Early diagnosis and management of kidney disease can delay or prevent the development of ESKD and minimize CKD mortality, through the management and treatment of complications associated with CKD such as, cardiovascular disease, hypertension, anemia, decreased quality of life and metabolic bone disease. [42, 48, 50]

CKD is under-recognized and under-diagnosed. In the National Health and Nutrition Examination Survey (NHANES) (1999 - 2000), 2% of US adults age 20 and older reported having a history of weak or failing kidneys [8]. Furthermore, less than 20% of people with moderate CKD (Glomerular filtration rate (GFR) of 30 to 59 ml/min per 1.73 m^2) and the presence of albuminuria reported knowing they had weak or failing kidneys (18.2%) [8]. This lack of CKD recognition is of concern for patients and clinicians. A previous study reported primary care physicians did not include ICD-9 diagnostic codes for CKD for 89% of patients with moderate CKD (GFR of 30 to 59 ml/min per 1.73 m^2) [51]. To improve CKD diagnosis and awareness, the National Kidney Foundation (NKF) implemented several education programs and clinical recommendations, including the automatic reporting of estimated Glomerular Filtration Rate (eGFR).[52]

The implementation of automatic eGFR reporting elicited debate among health professionals about its utility and role in the early detection and management of CKD. One view maintains that automatic eGFR reporting will provide kidney function assessments directly to physicians who previously had to calculate eGFR by hand using estimating equations. This simplification of the reporting of eGFR may lead to an increased awareness of CKD among physicians and other health professionals and earlier identification of patients for the initiation of treatment of CKD. An opposing view argues that automatic eGFR reporting will be used as a population-level screening program for CKD, which could result in increased diagnoses of CKD, for patients who may never progress to ESKD. However, there is no scientific evidence to adequately identify CKD patients that will progress to ESKD, and the therapeutic interventions available to slow the progression from CKD to ESKD must be implemented during the early disease stages.

Although the utility and role of automatic eGFR reporting remains unsettled, studies in international populations have shown that eGFR reporting have resulted in increased CKD detection, referrals, consults, and first time visits to nephrology clinics.[36-40] However, the impact of automatic eGFR reporting policies on CKD awareness, detection, and treatment warrant further investigation in US populations. In April 2005, the University of North Carolina Healthcare System (UNCHS) voluntarily implemented a system-wide CKD initiative that includes the automatic reporting of eGFR, calculated using the Modification of Diet in Renal Disease (MDRD) equation on all serum creatinine tests ordered. The goal of this initiative was to facilitate the early diagnosis of CKD and improve early medical management to minimize CKD burden among UNCHS patients. In the years since this initiative began, the impact of this administrative decision has yet to be evaluated.

We sought to evaluate the impact of automatic eGFR reporting within UNCHS on the identification of CKD patients and nephrology referrals within the UNC Nephrology clinics between the years 2004-2010. The aims to address the study focus are detailed below.

Specific Aim 1: Impact of eGFR reporting on CKD detection among at-risk population

To quantify the detection of CKD detection prior to and following the implementation of automatic eGFR reporting among adults patients *who had at least one SCr measurement with an eGFR measurement below 60ml/min/1.73m^2* seen in the UNC Healthcare System (UNCHS) between January 2004 and December 2010.

Hypothesis: CKD detection will increase by at least 10% from before to after the implementation of automatic eGFR reporting in April 2005.

Rationale: To determine if eGFR reporting helps increase the detection of CKD among adults at-risk for CKD detection in the UNC Healthcare System (UNCHS).

Specific Aim 2: Impact of eGFR reporting on adherence to National Kidney Foundation CKD guidelines

To quantify the proportion of adults who *had a second SCr measurement after an initial eGFR <60 ml/min/1.73m^2* before and after the implementation of automatic eGFR reporting seen in the UNC Healthcare System (UNCHS) between January 2004 and December 2009,

Hypothesis for Aim 2: Adherence to CKD guidelines will increase by at least 10% from before to after the implementation of automatic eGFR reporting in April 2005.

Rationale: To quantify the proportion of adherence to CKD guidelines among the sub-population of at-risk CKD patients.

Specific Aim 3: Impact of eGFR reporting on the clinical diagnosis of CKD given two eGFR measurements <60ml/min./1.73m^2.

To quantify the detection of clinically identified CKD before and after the implementation of automatic eGFR reporting among adult patients with lab-verified moderate to severe CKD (i.e. ***two eGFR measurements below 60ml/min/1.73m^2)*** seen in the UNC Healthcare System (UNCHS) between January 2004 and August 2009.

Hypothesis for Aim 3: Diagnostic labeling of CKD in patients with two eGFR measurements below (60ml/min./1.73m^2) will increase by at least 10% from before to after the implementation of automatic eGFR reporting in April 2005.

Rationale: To quantify CKD detection among adults with lab-verified CKD in the UNC Healthcare System (UNCHS).

Specific Aim 4: Impact of eGFR reporting on referrals to nephrology

To examine the proportion of nephrology referrals to UNC Nephrology clinics for adult patients with stage 3 CKD or higher before and after the implementation of automatic eGFR reporting in the UNCHS

Hypothesis for Aim 4: Referrals to a nephrologist will increase by 25% after the implementation of automatic eGFR reporting compared to before automatic eGFR reporting.

Our study sought to expand the current body of chronic kidney disease detection research and to gain a greater understanding, of how automatic eGFR reporting impacts detection and patient care. It also sought to identify which sub-populations eGFR reporting benefitted most in terms of detection and referral to help provide a foundation upon which public health, medical professionals and policy makers can inform future clinical recommendations for screening, detection and patient care for CKD.

CHAPTER THREE: RESEARCH PLAN AND METHODS

Study Design Overview

To examine how automatic eGFR reporting in hospitals and clinical practices impact CKD detection and care management, we conducted a data analysis of administrative claims data and electronic medical records from the University of North Carolina Hospital System (UNCHS).

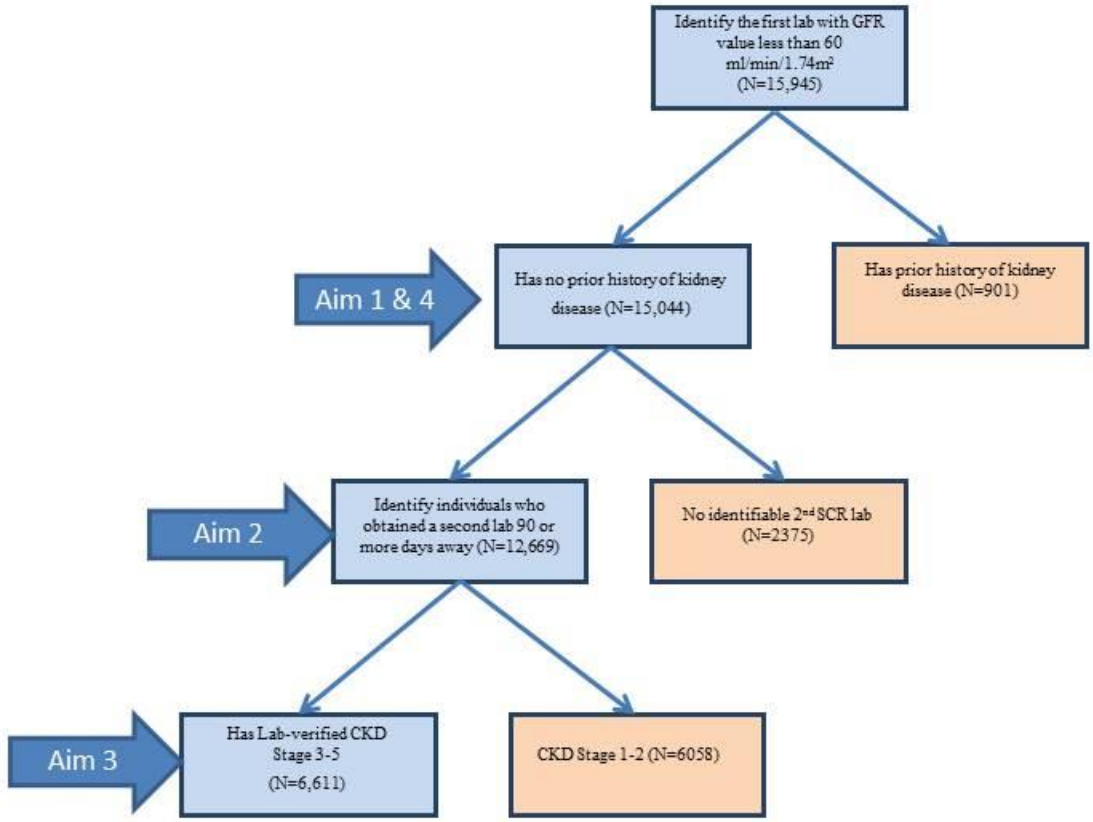
Study Setting

Participants for this cross-sectional study were selected from the University of North Carolina Hospital System (UNCHS). UNCHS is a state owned integrated not-for profit healthcare system based in Chapel Hill, NC. This academic medical center provides services for children, women, psychiatric and neurologic patients, and general adult patient care. UNCHS provides service to patients regardless of their ability to pay. There are currently about 2,000 faculty physicians and physicians-in-training providing care for UNCHS patients. Of the 400,000 UNCHS patients seen in 2009, 55% were women, 42% were minority, and 10% were uninsured. UNCHS provides care for patients from all 100 counties of North Carolina, with the top counties being Orange, Wake, Alamance, Durham, Chatham and Cumberland counties, and also served patients from multiple Southeastern US states.

Study Population

This study included adult patients, age 18- 70, who were seen in the UNCHS between January 1, 2005 and December 31, 2010 and had at least one serum creatinine measurements and no previous history of kidney disease. Patient race, sex, and a serum creatinine measurement are required to assess eGFR. Therefore, patients with an unknown race or sex, or a missing a serum creatinine lab were also excluded from the study. 15,945 patients with at least one low eGFR measurement less than 60/ml/min/1.73m^2 were identified. Nine hundred and one were excluded due to having a history of kidney disease, leaving 15,044 patients in the base study population. For Aim 2, two thousand three hundred and seventy-five patients were excluded because there was no identifiable 2nd SCr lab. Six thousand fifty-eight were excluded because they did have not moderate to severe CKD (GFR>60 mL/min/1.73m2). (Figure 1)

Figure 1: Study Exclusion Criteria



Data Source

Administrative claims data was obtained from the WebClinical Information Systems (WebCIS), the laboratory information system, an accounting system and the UNC Physicians and Associates (UNC P&A) Billings data. WebCIS is a repository of electronic medical records developed in 1992 to help facilitate access to all UNCHS medical records and to allow patients to be followed in both in-patient and out-patient settings.[53] Clinical and administrative information such as patient demographics, laboratory and pathology results, medical imaging and prescribed medications are currently available in WebCIS. Clinical information from WebCIS was linked to the laboratory information system coordinated by McClendon Clinical

Laboratories. This system coordinates and integrates all UNHS Clinical Laboratory and Anatomic Pathology services including serum creatinine labs. The patient's International Classification of Diseases (version 9) (ICD-9) diagnoses came from Trendstar, a McKesson Information System accounting system, used in the UNCHS to coordinate billing and insurance claims for all patients. Information about scheduled nephrology appointments were obtained from the UNCHS Appointment scheduling system and diagnosis information for the study were obtained from UNC P&A data files. UNC P&A is the billing department for UNC faculty practice within the Healthcare system.

Data Acquisition and Creation

Project data was abstracted by the North Carolina Translational Science Institute (NCTRaCS), Clinical Data Warehouse for Health (CDW-H). CDW-H is a biomedical informatics resource that manages and mines all UNC Hospital clinical and research data, ranging from billing and insurance to diagnosis and medication information. It was established in 2008 to enhance the quality of care and clinical research with the UNCHS patient population. CDW-H contains data from clinical and operations systems within UNCHS, primarily from WEBCIS. After CDW-H project requests was submitted to the governance committee and approved the requested research data was made available to the study investigators.

NCTRACS queried the UNCHS records to identify all SCr labs between January 1, 2004 and December 31, 2010. 1,643,782 labs were identified. The study investigator identified and flagged all individuals (N= 82,645) that had at least two SCr labs 3 months apart. Identified

patient ids were sent back to NCTRaCS to obtain patient characteristics, lab results, provider information, and health status/ co morbidities. Nephrology appointment data was obtained from UNC P&A appointment scheduling system, to identify whether or not patients were scheduled an appointment after a low eGFR value. The data files sent to obtain study data are listed below. Additional description of the excel files that were sent are described in detail in Appendix 1.

- DX (Contained all diagnosis identified for patients in UNCHS)
- Postal Code (Contained information on the billing addresses for patients.)
- Demog (Contained the race, date of birth, gender of patients in UNCHS)
- Lab (Contained that laboratory results for the GFR labs)
- Outpatientvisits (identified the clinic the patient was seen in during the UNCHS visit)
- Payor (Identified the billing payor for the UNCHS visit)
- Problems (identified patient's comorbidities listed in the medical record)
- Visits (identified the inpatient admission information for the corresponding UNCHS visit)
- NephAppts (identified the scheduled nephrology appointments for the corresponding UNCHS visit)
- NephVisits (Contained hospital billing data for Nephrology clinic visits earlier than 12/31/2010)
- NephVisitInsurers (Contained patients' insurance data for Nephrology clinic visits earlier than 12/31/2010)

After the acquisition of the data files from NCTRACS, each excel data file was converted to a SAS data file. The files were combined using the unique identifiers that connect each data set. The identifiers used for each data set are disclosed in Appendix Table 1.

Study Variables

Laboratory Verified Chronic Kidney Disease (Aim 1)

Prior to the automatic reporting of eGFR in 2005, GFR was calculated manually using the abbreviated Modification of Diet in Renal Disease (MDRD) equation.[29] This study calculated GFR for those patients seen prior to the implementation of the automatic reporting, before April 2005. For those patients with clinic visits after April 2005, eGFR was abstracted from WebCIS as automatically reported patient their lab results. Individuals with two eGFR measures below 60mL/min/ $1.73m^2$ were classified as having ***laboratory verified CKD***. Individuals for whom one or both of the eGFR values were above 60mL/min/ $1.73m^2$ were classified as having normal kidney function.

Assessment of CKD detection (Aim1)

For patients identified as having laboratory verified CKD, the medical record corresponding to the second SCr lab result was examined for any indication of CKD diagnosis via ICD-9 codes in the discharge report. If any of the CKD codes in Table 2 were indicated in the discharge records then the patient was labeled has having ***detected CKD***. If no indication of a CKD diagnosis was present in the discharge record, then the patient was identified as having ***undetected CKD***.

Table 2- Diagnosis Codes used for the Definition of Chronic Kidney Disease Documentation

Chronic kidney disease	585 or 585.1- 585.5
Proteinuria	791.0
Unspecified disorder of kidney and ureter	593.9
Hematuria	599.7
Malignant hypertensive renal disease with renal failure	403.01
Benign hypertensive renal disease with renal failure	403.11
Unspecified hypertensive renal disease with renal failure	403.91
Malignant hypertensive heart and renal disease with renal	404.02
Malignant hypertensive heart and renal disease with heart	404.03
Benign hypertensive heart and renal disease with renal	404.12
Benign hypertensive heart and renal disease with heart	404.13
Unspecified hypertensive heart and renal disease with renal	404.92
Unspecified hypertensive heart and renal disease with heart	404.93

Assessment of scheduled nephrology appointment (Aim4)

Patients must be referred by a physician in order to be seen by a nephrologist. However, due to the limited capabilities of the medical records, referrals to nephrologist outside of the UNCHS are not consistently captured. For the purposes of this study the information regarding referrals will only apply to those nephrologists in the UNCHS and defined as having a scheduled nephrology appointment. The appointment scheduling system was queried to determine if patients had any nephrology appointments scheduled after the flagged low eGFR. If an appointment was identified then the patient was labeled as having a scheduled appointment; if no identified appointments were identified, they were labeled as no labeled appointment.

Changes in CKD Function (Aim 4)

For those with a scheduled nephrology appointment laboratory records were searched to identify follow-up SCr measurements during the 12 months following the initial nephrology visit. Laboratory records were also searched for SCr measurements over 12 months following the initial laboratory value for patients who did not have a scheduled nephrology visit. Change in CKD function was based upon these subsequent lab values and categorized as No Change, Increase in Stage (deterioration of kidney function) and Decrease in Stage (improvement of kidney function). No change was defined as those who had no change in their subsequent GFR level compared to the initial lab; an increase in staging was defined by the decrease in GFR levels in the subsequent lab when compared to the initial lab. For example a reduction in GFR from 15-29mL/min/1.73m^2 to <15mL/min/1.73m^2 would be categorized as an increase in stage. Lastly, a decrease in stage is when the subsequent GFR level is higher than the initial GFR lab value. For example an individual whose initial lab value is 15-29mL.min/1.73m$^{2\ but}$ has a subsequent lab value one year later that increases to 30-59 mL/min/1.73m^2, they would be categorized as decrease in stage.

Exposure: Timing of Healthcare Visit

The exposure of interest was the ***timing of the healthcare visit,*** determined by whether or not the patient was seen in the UNCHS before or after the implementation of the automatic eGFR reporting. If the service date of the patient's UNC Hospital visit was between the dates January 1,2004 and April 30, 2005, inclusive, then the patient was seen prior to the implementation of the automatic eGFR reporting and are considered unexposed. However,

patients were considered exposed if they were seen at UNCHS between the dates May 1, 2005 and December 31, 2010, after the implementation of the automatic eGFR reporting.

Additional variables

This study also examined patient demographics, health status/co-morbidities, and provider information. These covariates were abstracted from the medical records and accounting system data. See Appendix 2 for description of each study covariate, data source, variable type, and categorization, if applicable. Patient's family history of kidney disease and socioeconomic status were not captured in the medical record and were not being examined in this study.

Data Analysis

Tabular analyses were used to examine the frequency of patient characteristics overall and separately within the eGFR reporting period. Crude associations between eGFR reporting period and study outcomes were examined using contingency tables. Associations between eGFR reporting periods and CKD detection were assessed using linear risk regression models and log-risk regression models. Multiple logistic regression was used to examine the effect of automatic eGFR reporting on scheduled nephrology appointments. Ordinal tests of association within strata were conducted to examine associations between reporting period and changes in CKD stage stratified by initial CKD stage. Effect measure modification and confounding were assessed and accounted for in final analyses.

To identify characteristics associated with CKD detection, scheduled nephrology appointments and changes in GFR, bivariate relationships between each outcome and each covariate were examined overall and by eGFR reporting period. A nominal level of statistical significance of 0.05 was used to identify associations with covariates. All analyses were conducted using SAS software (version 9.2, SAS Institute, Cary, NC).

CHAPTER FOUR: PAPER 1- AUTOMATIC EGFR REPORTING AND DETECTION OF CHRONIC KIDNEY DISEASE

Background

Persistent kidney dysfunction, known as CKD, is an ever growing issue plaguing society. CKD prevalence has increased 30%, from 10.1% in 1988-1994 to 13.1% in 1999-2004 [1]. While accurate estimates of CKD stages 1-4 are not available, the incidence of Stage 5 CKD, or end-stage kidney disease (ESKD), increased from 86.2 per million population in 1980 to 350.8 per million population in 2008. The care of ESKD patients consumes roughly 6% of the US Medicare budget [54]. CKD and ESKD lower a patient's quality of life and causes economic burden on individuals, health care systems and society[20]. However, with early detection and treatment of CKD can be successful in slowing the onset and progression to ESKD [3, 8, 24-27].

Despite the high burden of CKD, awareness and detection of kidney disease in the US is low among consumers and providers of health. [8, 55-59]. According to the 2004 NHANES survey less than 10 percent of US adults with moderate (eGFR of 30 to 59 mL/min/1.73m^2) and 24% of those with severe (eGFR of 15 to 29 mL/min/1.73m^2) kidney dysfunction report ever being detected, or told that they have weak or failing kidneys[8]. Similarly, in a large US managed care cohort (> 10,000 people), only 14% of patients with eGFR <60 mL/min/1.73 m^2 were documented as having CKD [60]. A cross-sectional study of adults over 40 years old reported that primary care physicians did not include International Classification of Diseases Version 9 (ICD-9) diagnostic codes for CKD for 89% of these patients with moderate CKD. [51].

Many international and US-based healthcare organizations and laboratories implemented policies that automatically report eGFR when SCr is measured [34, 61, 62], eliminating the time and effort of manual calculations. Studies of international populations have shown that automatic eGFR reporting resulted in increased CKD detection, referrals, consults, and first time visits to nephrology clinics [36-40]. In contrast, the impact of eGFR reporting in US healthcare systems remains unclear [34, 61, 62].

On April 27, 2005 the University of North Carolina Healthcare System (UNCHS) implemented a system-wide CKD initiative to report eGFR automatically, using the MDRD equation, on all patients ≥ 18 years of age who underwent SCr measurements. Two memoranda were distributed and dissemination sessions were held to inform all health care providers in the system of this initiative. The goal of the automatic eGFR reporting initiative was to increase reporting efficiency, facilitate the early diagnosis of CKD, and improve early medical management to minimize CKD burden among UNCHS patients. We evaluated whether eGFR reporting improved detection and CKD awareness in a public tertiary US hospital system and determined which demographic factors and comorbid conditions were associated with CKD detection.

Methods

All inpatients and outpatients 18 to 70 years of age who received services at the UNCHS between January 2004 to August 2009, and had at least one eGFR value less than 60 mL/min/1.73m^2 were selected for inclusion in this study (n=15,945). Patients were excluded if they: (1) had, prior history of kidney disease (N=901); (2) no identifiable 2nd SCr measurement

(N=2375); and (3) eGFR > 60 mL/min/1.73m^2 (N= 6058) after the 2nd SCr measurement (Figure 2).

Medical record and laboratory data were extracted from the electronic health record at the UNCHS's Web Clinical Information System. Diagnoses and procedures coded by ICD-9 were obtained from Trendstar, an accounting system used for billing and insurance claims. The institutional review board of The University of North Carolina School of Medicine, as well as the UNC Hospital Governance Board for access to the UNCHS data approved this study.

Medical records were used to determine race/ethnicity and age at initial clinic visit. Comorbidities were labeled based upon the presence of at least one ICD-9 code in the medical record within one year prior to the date of the initial low eGFR measurement. The comorbidities and corresponding ICD-9 codes included: diabetes mellitus (250.x); essential hypertension (401.x, 402.x); and cardiovascular disease (CVD) (410.x-414.x, 428.x, 429.2, 430-438). Patient's health insurance was determined as the last known insurance identified in the medical records and categorized as private (Blue Cross/ Blue Shield, CHAMPUS, commercial insurance carriers and HMO/PPO), public (Medicaid, Medicare A or Medicare B), or no insurance. Patients with worker's compensation or whose medical care was paid for by UNC were classified as having no health insurance coverage. Ease of access to healthcare was calculated as the number of miles between the patient's billing address and the UNC clinic location.

The eGFR reporting period was determined by the timing of the patient's UNCHS visit relative to the implementation of the automatic eGFR reporting initiative in the UNCHS. The eGFR reporting period was considered pre-initiative if the service date of the patient's UNCHS

visit was between January 1, 2004 and April 27, 2005 inclusive, and post-initiative if the UNCHS visit was after April 27, 2005. The eGFR was manually calculated for patients seen prior to the implementation of automatic reporting (January 2004 and April 2005) using the MDRD equation[29]:

eGFR= 186*[SCr]-1154*[age] -0.203 *[0.742 if female]*[1.212 if African American] .

For patients whose clinic visits/admissions occurred after April 2005, eGFR was abstracted from the electronic health record. Individuals with two eGFR measures below 60mL/min/ 1.73m^2 were classified as having laboratory verified CKD. Individuals for whom one or both of the eGFR values are above 60mL/min/ 1.73m^2 were classified as not having CKD and thus excluded from this study.

The UNCHS medical records were searched for detected CKD, defined as having at least one discharge ICD-9 code of 585.x within one year of the lab date. If no indication of CKD diagnosis was identified in subsequent medical records after one year then the patient was labeled as undetected CKD. The date of the first visit with an ICD-9 code indicating CKD was considered the detection date. The one-year CKD detection rates were determined before and after eGFR reporting for the study cohort.

Statistical Analysis

Tabular analyses were used to examine the frequency of patient characteristics overall and separately within the eGFR reporting period. Crude associations between eGFR reporting

period and CKD detection were examined using contingency tables. Linear risk regression models were used to estimate the 1 year cumulative incidence (CI) and difference (CID) of CKD detection in the study cohort pre- and post-initiative. Log-risk regression models were used to estimate the incident risk ratios (RR) and 95% Confidence Intervals (CI) pre- vs. post initiative. Effect measure modification and confounding were assessed and accounted for in final analyses.

To identify characteristics associated with CKD detection, bivariate relationships between CKD detection and each covariate were examined overall and by eGFR reporting period. Significantly associated covariates ($p<0.05$) were simultaneously entered into an adjusted multivariate linear risk model; univariate and adjusted cumulative incidence of detection ratios (CIR) and 95% confidence intervals were presented. All analyses were conducted using SAS software (version 9.2, SAS Institute, Cary, NC).

Results

We identified 6,611 patients with 2 low eGFR values (< 60 ml/min/1.73m^2). Overall, the majority of this study's population were identified as having eGFR levels of 30-59 mL/min/1.73m^2 (74%), female (57%), white (59%), and over the age of 40 (90%). Forty-nine percent of the patients had a history of hypertension, 25% had a history of diabetes and 20% had a history of CVD. Private health insurance was reported in 36% of patients, and most study patients travelled less than 50 miles to UNCHS for care (66%) while 35% travelling less than 20 miles (Table 3).

The characteristics of the cohort of individuals seen prior to the reporting initiative are similar to those seen in UNCHS post-initiative, with some exceptions. There was a higher proportion of individuals with comorbidities post-initiative, compared to pre-initiative (hypertension (55% vs. 35%), diabetes (28% vs. 19%) and CVD (24% vs. 13%)). While most patients had public and or private health insurance, more pre-initiative patients were missing health insurance information compared to post-initiative patients (19% vs. 0.01%, respectively) (Table 3).

Of the 6,611 patients in the study, 16.6 % (n=1096) were labeled as having detected CKD within one year of lab-verified CKD date. More were detected after the implementation of eGFR reporting (15.6% pre-initiative vs. 17.1% post-initiative). No effect measure modification or confounding was identified for detection of CKD by hypertension, diabetes, gender, race, age, CVD, insurance, or distance to UNCHS.

Stratified analyses were conducted to examine sub-groups that may benefit from eGFR reporting. Detection rates after the eGFR reporting initiative were found to be significantly higher than the rates before reporting initiative for those with moderate CKD (Stage III eGFR of 30-59 mL/min/1.73m^2), older age, males, Whites, and those with comorbidities. Individuals with moderate CKD had a detection rate that was 131% higher post eGFR reporting than pre-initiative (CID=2.31; 95% CI: 1.89, 2.82). Detection rates were 48% higher post eGFR reporting initiative than before reporting for those age 60-70 years (CID=1.48; 95% CI: 1.195, 1.86). Males and Whites were detected at a 19% and 35% higher rate, respectively, post-initiative than pre-initiative (males CID=1.19; 95% CI: 1.01, 1.40; whites CID=1.35; 95%CI: 1.18, 1.63). Individuals with a history of diabetes (CID=1.37; 95% CI: 1.08, 1.76), hypertension (CID=1.31;

95% CI: 1.08, 1.59) and CVD also had a higher detection rate post-initiative than pre-initiative (Table 4).

When examining the diffusion of innovation effect on CKD detection among the sub-populations that benefited from eGFR reporting, we determined that the greatest increase in CKD detection within these groups occurred during the 2nd and 3rd years after implementation (Figure 3 and Table 5). However, this increase in detection was not sustained thereafter; with a decline in the CKD detection rates for most groups back to the initial CKD detection rate pre-initiative.

Factors found to be independently associated with CKD detection pre-initiative were eGFR (<0.001), older age (<0.001), race (0.025) and sex (0.0067) (Table 6). In reference to eGFR levels, those with eGFR levels of 15-29 mL/min/1.73m^2 and eGFR <15 mL/min/1.73m^2 were significantly more likely to be detected than those who had an eGFR 30-59 mL/min/1.73m^2 (CIR=4.27; 95% CI: 3.32, 5.48; and CIR=7.31; 95% CI: 5.87, 9.09 respectively). African Americans were 2.23 times as likely to be detected as Whites (CIR=2.23; 95%CI: 1.82, 2.74), and females were less likely to be detected than males pre-initiative (CIR: 0.76; 95%CI: 0.62, 0.93).

Similar factors were found to be independently associated with CKD detection post-initiative: eGFR level (0.0035), race (0.0013), and sex (<0.001). In addition, hypertension (0.0027), diabetes (<0.001) and CVD (<0.001) were also associated with CKD detection post-initiative. Those with an eGFR 15-29 mL/min/1.73m^2 (stage IV) were 1.96 times more likely to be detected than those with moderate (stage III) eGFR level (CIR=1.96; 95% CI: 1.67, 2.29). African Americans were 58% more likely to be detected than whites (CIR=1.58; 95% CI: 1.38, 1.80). Additionally those factors found to be associated post-initiative were history of CVD

(CIR=1.48; 95% CI: 1.30, 1.70), diabetes (CIR=1.52; 95%CI: 1.33, 1.73), and hypertension (CIR=1.22; 95% CI: 1.07, 1.40) as shown in Table 6.

Discussion

We examined the effect of automatic eGFR reporting on CKD detection rates in a Southeastern USA tertiary referral center and found that automatic eGFR reporting moderately increased the overall detection of CKD by approximately 9%. More significantly, among those with moderate CKD (Stage III, eGFR: 30-59 mL/min/1.73m^2), there was an increase of 131% CKD detection after the implementation of eGFR reporting. We found that older age, male gender, white race and a history of hypertension, diabetes or CVD were associated with an increase in CKD detection after implementation of eGFR reporting when compared to pre-initiative reporting. We also identified the eGFR reporting initiative had the greatest impact of CKD detection during the second year of implementation, but the increase in CKD detection was not sustained. Lastly, we found that eGFR level, age, race, and sex were independently associated CKD detection both pre-initiative and post-initiative. We also found that having comorbidities was independently associated with post automatic eGFR reporting.

The increase in detection among those with moderate CKD indicates that eGFR reporting potentially benefits those who may have otherwise gone undetected until reaching more advanced stages of CKD. The association between African American race and CKD detection was also noted in a previous study of in-patients only at UNCHS during a similar study period

[63]. This may indicate that health providers are aware that CKD disproportionally affects this minority group, but in contrast with other reports [26], we did not detect a sex difference.

Most studies that have examined the impact of automatic eGFR reporting have shown that implementation resulted in increased CKD detection rates. A US based Veteran Affairs study showed a 7% improvement in CKD detection; however overall CKD detection was low with only 10% of those with stage III (eGFR 30-59 min/mL/m^2) identified [64]. A study of hospitalized elderly patients showed that there was a significant increase in CKD detection after implementation of eGFR reporting, although there was no change in physician prescribing patterns [61]. Similarly, a United Kingdom-based study reported an increase in detection after the implementation of eGFR reporting [65].

As in previous reports [9, 60, 62], we found that overall CKD detection rates were low, emphasizing the need to develop ongoing efforts to educate health professionals. Studies by Akbari et al. and Richards et al, showed that provider education and care management techniques coupled with the implementation of eGFR reporting improves the identification rate of CKD [66, 67]. Although some efforts were taken to inform providers of the implementation of automatic eGFR reporting in the UNCHS, no well-defined provider education program was established, which may have contributed to the unexpected decrease in CKD detection after eGFR reporting started.

Our study limitations include a potential misclassification of CKD. Current CKD guidelines define CKD as persistent kidney dysfunction with or without the presence of kidney

damage. Automatic eGFR reporting only assesses kidney dysfunction through serum creatinine measures and not the presence of protein in a patient's urine. Patients with kidney damage who would meet clinical criteria for CKD were not identified in our study. ICD-9 codes are often used to identify CKD and related conditions (e.g. proteinuria and nephrotic syndrome). Use of the latter codes may capture additional patients with CKD, but would also increase misclassification of CKD. Thus, we chose to define CKD using ICD-9 code 585 to ensure the ascertainment of CKD labeling and not that of other related kidney diseases.

A further limitation of this report is that, information was only available for the 15 months prior to the implementation of the automated eGFR reporting. The short timeframe for pre-eGFR reporting may have constrained our ability to estimate the true detection of CKD prior to automated eGFR reporting. The time available for identification of comorbidities and patient characteristics was limited to one year prior to the clinic visit date associated with the second low eGFR measurement, pre- and post- initiative, to minimize differential misclassification with respect to eGFR reporting period.

UNCHS is a referral center, and it is possible patients may have had a second low eGFR measurement assessed at a center external to UNCHS, and thereby received a diagnosis of CKD prior to UNCHS's documentation of a second low eGFR. A sensitivity analysis was conducted to examine the risk of CKD detection among patients after their first low eGFR value. Results from the sensitivity analyses indicated similar detection patterns as those in the overall study, with a lower CKD detection post-initiative reporting, than pre- initiative reporting. The detection rates

among this group did not differ with respect to magnitude or direction. Thus, selection bias due to the definition of lab-verified CKD should not significantly alter these results.

Beyond the aforementioned limitations, this study has several strengths. The database includes a combination of hospital and patient level data for a large sample of individuals within a US based tertiary care hospital system. The UNCHS provides care for a racially and economically diverse population of patients. The distribution of the overall sample population with 33% being African American and a fairly equal distribution of those with public vs. private insurance is consistent with both the general population of NC and the general demographics of the patients cared for the UNCHS.

We observed that the implementation of automatic eGFR reporting slightly increased the identification of individuals with CKD within a tertiary healthcare system. As the post-initiative rate of detection remained low, these data suggest an opportunity to increase education and awareness about eGFR among healthcare professionals. Examining whether changes in referral patterns to nephrologists occurred following the introduction of automated eGFR reporting remains an important clinical practice question.

Figure 2 Study Population Exclusion/ Inclusion Flow Chart

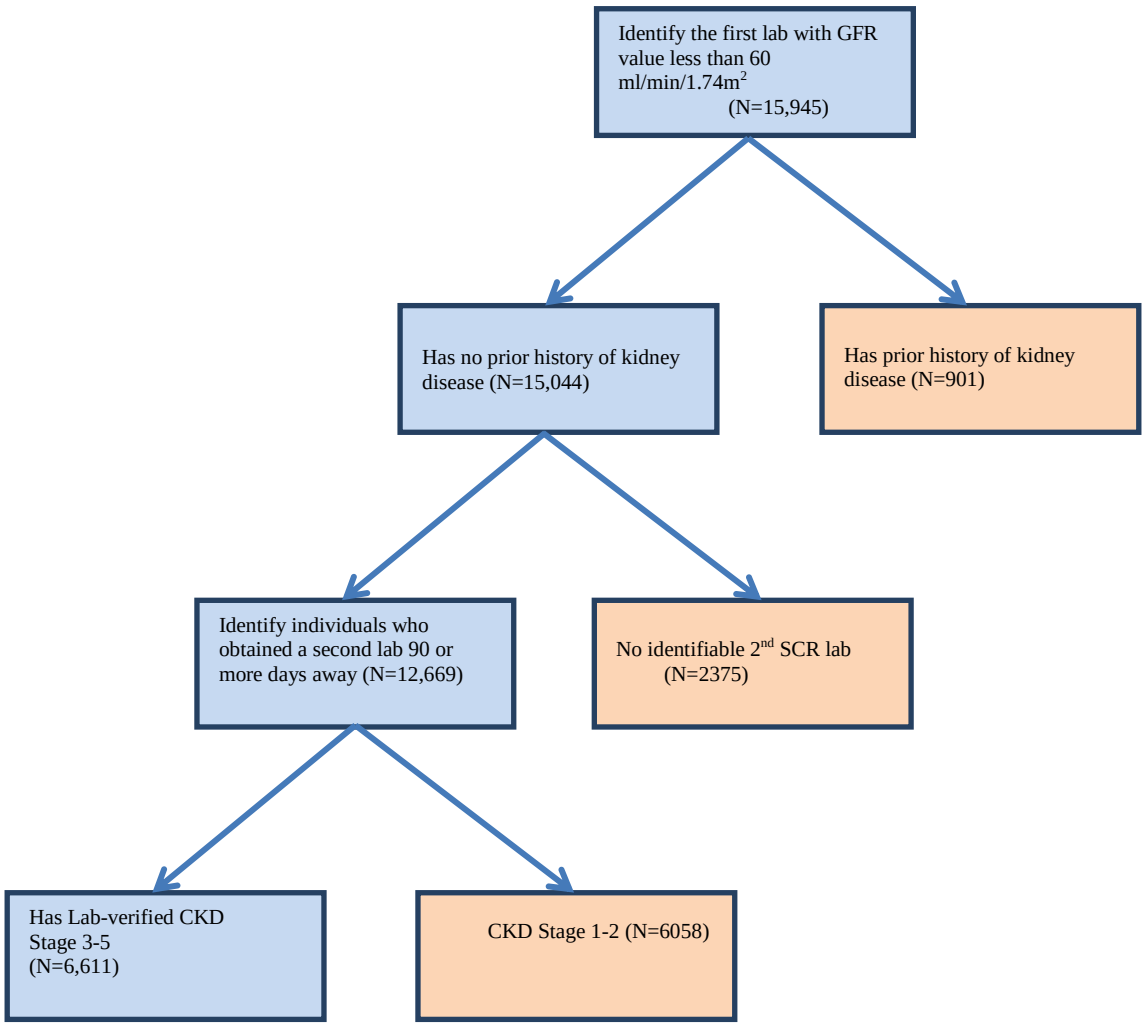


Table 3-Characteristics Of Lab-Verified CKD Patients (2004-2010) At the UNCHS
(Overall and by eGFR Reporting Period)

Characteristics	*Overall (N=6611)*	Pre-Initiative Jan2004-April 2005 (N=2119)	Post-Initiative May 2005-Dec 2009 (N=4492)
	N %	N %	N %
eGFR level[†] 30-59 mL/min/1.73m^2	4,880 (73.8)	1,554(73.3)	3,326(74.0)
15-29 mL/min/1.73m^2	755 (11.4)	307(14.5)	448(10.0)
<15 mL/min/1.73m^2	976 (14.8)	258(12.2)	718(16.0)
Males	2,866 (43.4)	928(43.8)	1,938(43.1)
Females	3,745 (56.6)	1,191(56.2)	2,554(56.9)
Whites[‡]	3,884 (58.8)	1,207(57.0)	2,677(59.6)
African-Americans	2,159 (32.7)	775(36.6)	1,384(30.8)
Other race	568 (8.6)	137(6.5)	431(9.6)
18-39 years of age	675 (10.2)	260(12.3)	415(9.2)
40-59 years of age	3,049 (46.1)	953(45.0)	2,096(46.7)
60-70 years of age	2,887 (43.7)	906(42.8)	1,981(44.1)
Hypertension[§]	3,212 (48.6)	748(35.3)	2,464(54.9)
Diabetes[§]	1,672 (25.3)	397(18.7)	1,275(28.4)
Cardiovascular disease[§]	1,349 (20.4)	268(12.6)	1,081(24.1)
No Health Insurance**	552 (8.3)	130(6.1)	422(9.4)
Public Insurance	2,182 (33.0)	687(32.4)	1,495(33.3)
Private Insurance	2,373 (35.9)	659(31.1)	1,714(38.2)
Public & Private Insurance	1,026 (15.5)	240(11.3)	786(17.5)
Missing Health Insurance information	478 (7.2)	403(19.0)	75(1.7)
Miles traveled to UNC: Less than 20 miles[***]	2,307 (34.9)	691(32.6)	1,616(36.0)
20-49 miles	2,048 (31.0)	617(29.1)	1,431(31.9)
50-99 miles	1,291 (19.5)	410(19.3)	881(19.6)
More than 100 miles	589 (8.9)	171(8.1)	418(9.3)
Missing Distance	376 (5.7)	230(10.9)	146(3.3)

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*All data were derived from UNC Healthcare System data for 2004-2010. The study population included patients with lab verified CKD Stage 3 or higher during 2004-2010. Patients with unknown race, gender and age, and previous kidney disease were excluded. The eGFR reporting period was determined by the timing of the patient visit relative to the implementation of the automatic eGFR reporting initiative in the UNCHS before April 2005 (Pre-); after April 2005 (Post-).

† eGFR level was determined based on the abbreviated Modification of Diet in Renal Disease (MDRD) equation.

‡ Based on the race/ethnicity reported in medical record. 'Other' race includes all patients with race/ethnicity identified as American Indian, Asian/Pacific Islander, Hawaiian, or Other race.

§ Patients with comorbidities identified in medical records (via ICD-9 codes) at least once within one year prior to clinic visit were identified classified as having Hypertension (401,402); Diabetes (250, 250.5, and 250.5); CVD (410-414,428, 429.2, 430-438)

**Health insurance coverage was determined based upon the insurance that was identified in the medical records within 60 days of the visit. Private (Blue Cross, CHAMPUS, Commercial, HMO/PPO) Public (Medicaid, Medicare A, Medicare B), No Health Coverage (Self-Pay, Workers' Compensation). . Data are missing for patients with unknown insurance.

***Miles traveled to UNCHS based upon the distance between UNCHS and patient address

Table 4- Association Between eGFR Reporting Period and CKD Detection

Table	Overall N (%)	Pre-Initiative Jan2004-April 2005 N (%)	Post-Initiative May 2005-Dec 2009 N (%)	Cumulative Incidence of Detection Ratio[a] (95%CI)	P-value
	N %	N %	N %		
Overall	1,096 (16.6)	330(15.6)	766(17.1)	1.09(0.97,1.23)	0.1327
eGFR level[b]					
30-59 mL/min/1.73m^2	643 (13.2)	108(6.9)	535(16.1)	2.31(1.89,2.82)	<.0001
15-29 mL/min/1.73m^2	232 (30.7)	91(29.6)	141(31.5)	1.06(0.85,1.32)	0.5931
<15 mL/min/1.73m^2	221 (22.6)	131(50.8)	90(12.5)	0.25(0.20,0.31)	<.0001
18-39 years of age	158 (21.4)	79(29.0)	79(17.0)	0.58(0.44,0.77)	0.0001
40-59 years of age	569 (18.0)	162(16.5)	407(18.6)	1.13(0.95,1.33)	0.1612
60-70 years of age	369 (13.6)	89(10.3)	280(15.2)	1.48(1.19,1.86)	0.0006
Females	514 (13.7)	163(13.7)	351(13.7)	1.00(0.85,1.19)	0.9622
Males	582 (20.3)	167(18.0)	415(21.4)	1.19(1.01,1.40)	0.0350
Whites[d]	515 (13.3)	129(10.7)	386(14.4)	1.35(1.12,1.63)	0.0017
African-Americans	500 (23.2)	185(23.9)	315(22.8)	0.95(0.81,1.12)	0.5565
Other race	81 (14.3)	16(11.7)	65(15.1)	1.29(0.77,2.15)	0.3278
Hypertension[c]	564 (17.6)	106(14.2)	458(18.6)	1.31(1.08,1.60)	0.0063
Diabetes[c]	353 (21.1)	65(16.4)	288(22.6)	1.37(1.08,1.76)	0.0099
Cardiovascular disease[c]	290 (21.5)	45(16.8)	245(22.7)	1.35(1.01,1.8)	0.0415
Miles traveled to UNC: Less than 20 miles	367 (15.9)	107(15.5)	260(16.1)	1.04(0.84,1.28)	0.7166
Traveled 20 to 49 miles	375 (18.3)	101(16.4)	274(19.1)	1.17(0.95,1.44)	0.1391
Traveled 50 to 99 miles	209 (16.2)	59(14.4)	150(17.0)	1.18(0.90,1.56)	0.2348
Traveled more than 100 miles	72 (12.2)	18(10.5)	54(12.9)	1.22(0.74,2.03)	0.4248

[a] Cumulative Incidence Risk Ratios were estimated using Log-risk regression models (Post vs. Pre initiative risks)

[b] CKD Stage was determined based on the abbreviated Modification of Diet in Renal Disease (MDRD) equation.

[c] Patients with comorbidities identified in medical records (via ICD-9 codes) at least once within one year prior to clinic visit were identified classified as having Hypertension (401,402); Diabetes (250, 250.5, and 250.5); CVD (410-414,428, 429.2, 430-438)

d Based on the race/ethnicity reported in medical record. 'Other' race includes all patients with race/ethnicity identified as American Indian, Asian/Pacific Islander, Hawaiian, or Other race.

e Miles traveled to UNCHS based upon the distance between UNCHS and patient address

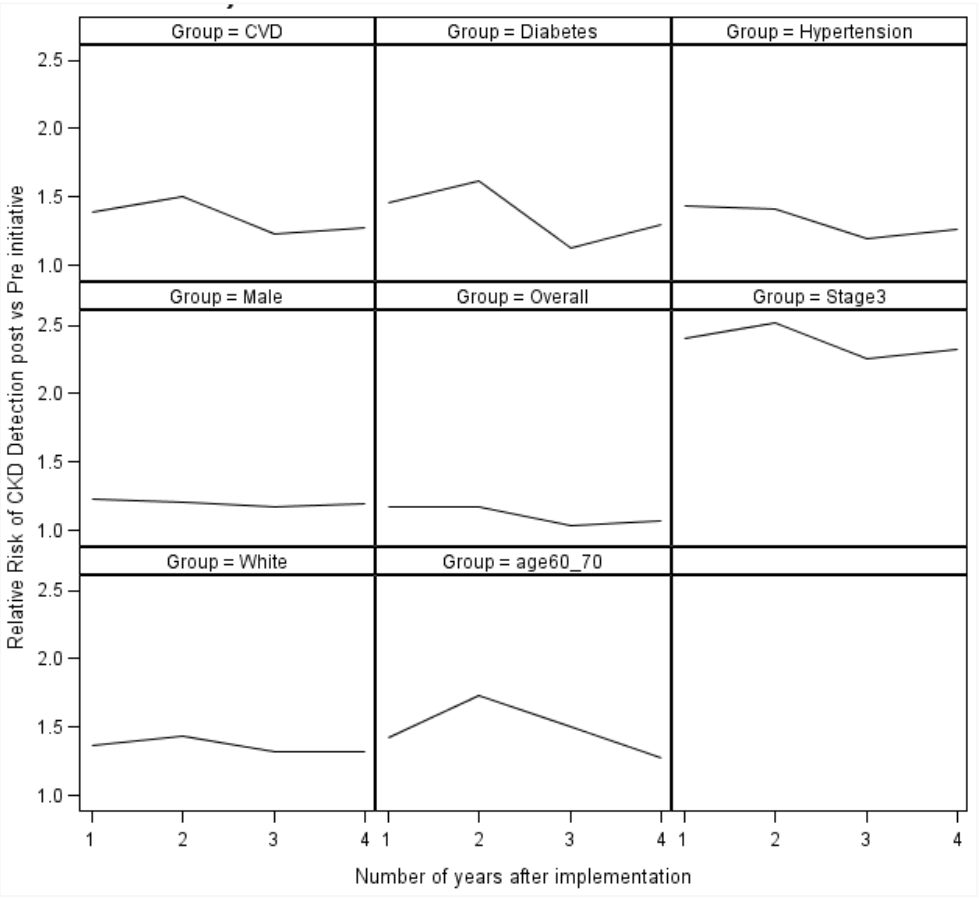
Table 5-Period Analysis: Stratified estimates of CKD Detection (Overall and according to eGFR reporting) Summary of Cumulative Incidence of Detection Ratio (95%CI) by Period

STRATIFIED GROUP	***ALL ELIGIBLE PATIENTS (N=6611)***	***1 year after reporting initiative* (N=3240)**	***2 years after reporting initiative* (N=3112)**	***3 years after reporting initiative* (N=3306)**	***4 years after reporting initiative* (N=3048)**
Overall	1.09(0.97,1.23)	1.17(1,1.37)	1.17(0.99,1.38)	1.03(0.88,1.22)	1.07(0.89,1.27)
CKD[a] Stage III: 30-59	2.31(1.89,2.8)	2.4(1.89,3.05)	2.52(1.98,3.21)	2.26(1.79,2.8)	2.32(1.8,2.99)
Age 60-70	1.48(1.19,1.86)	1.42(1.05,1.9)	1.73(1.3,2.31)	1.5(1.13,2)	1.28(0.92,1.78)
Male	1.19(1.01,1.40)	1.23(0.99,1.53)	1.21(0.96,1.53)	1.17(0.94,1.45)	1.2(0.95,1.51)
Whites	1.35(1.12,1.63)	1.37(1.07,1.76)	1.44(1.12,1.85)	1.32(1,1.68)	1.32(1.01,1.72)
Hypertension[b]	1.31(1.08,1.59)	1.43(1.1,1.81)	1.41(1.11,1.8)	1.2(0.94,1.54)	1.26(0.96,1.64)
Diabetes[b]	1.37(1.08,1.76)	1.46(1.08,1.96)	1.62(1.21,2.17)	1.13(0.82,1.56)	1.3(0.93,1.8)
Cardiovascular disease[b]	1.35(1.01,1.8)	1.39(0.99,1.95)	1.5(1.07,2.12)	1.23(0.87,1.75)	1.28(0.88,1.87)

[a]CKD Stage was determined based on the abbreviated Modification of Diet in Renal Disease (MDRD) equation.

[b] Patients with comorbidities identified in medical records (via ICD-9 codes) at least once within one year prior to clinic visit were identified classified as having Hypertension (401,402); Diabetes (250, 250.5, and 250.5); CVD (410-414,428, 429.2, 430-438)

Figure 3- Period Analysis: Stratified estimates of Relative Risk of CKD Detection



CKD= Chronic Kidney Disease
eGFR= estimated GFR

Table 6- Factors Associated With CKD Detection Before And After eGFR Reporting Period (Crude)

	Pre-Initiative Jan2004-April 2005		Post-Initiative May 2005-Dec 2009	
	Cumulative Incidence of Detection Ratio[a] (95%CI)	*p-value*	Cumulative Incidence of Detection Ratio[a] (95%CI)	*p-value*
eGFR level[b]	Ref.		Ref.	
30-59 mL/min/1.73m^2		<0.001		0.0035
15-29 mL/min/1.73m^2	4.27 (3.32, 5.48)		1.96 (1.67, 2.29)	
<15 mL/min/1.73m^2	7.31 (5.87, 9.09)		0.78 (0.63, 0.96)	
Age	Ref.		Ref.	
18 to 39 years		<0.001		0.9479
40 to 59 years	0.57 (0.45, 0.72)		1.10 (0.88, 1.37)	
60 to 70 years	0.35 (0.27, 0.46)		0.90 (0.71, 1.13)	
Race	Ref.		Ref.	
White		0.0025		0.0013
African American	2.23 (1.82, 2.74)		1.58 (1.38, 1.80)	
Other race	1.09 (0.67, 1.78)		1.05 (0.82, 1.33)	
Gender	Ref.		Ref.	
Male				<0.001
Female	0.76 (0.62, 0.93)	0.0067	0.64 (0.56, 0.73)	<.0001
No Cardiovascular disease	Ref.		Ref.	
Cardiovascular disease	1.09 (0.82, 1.45)	0.5541	1.48 (1.30, 1.70)	<.0001
No Diabetes	Ref.		Ref.	
Diabetes	1.06 (0.83, 1.36)	0.6249	1.52 (1.33, 1.73)	<.0001
No Hypertension	Ref.		Ref.	
Hypertension	0.87 (0.70, 1.07)	0.1908	1.22 (1.07, 1.40)	0.0027
Miles traveled to UNCHS:				
Less than 20 miles	Ref.	0.2867	Ref.	0.9809
20 to 49 miles	1.06 (0.82, 1.36)		1.19 (1.02, 1.39)	
50 to 99 miles	0.93 (0.69, 1.25)		1.06 (0.88, 1.27)	
More than 100 miles	0.68 (0.42, 1.09)		0.80 (0.61, 1.05)	
Health Insurance				
Private Insurance	Ref.	0.0513	Ref.	0.4088
Public Insurance	1.47 (1.14, 1.89)		1.20 (1.03, 1.39)	
Public and Private Insurance	1.32 (0.94, 1.87)		0.77 (0.62, 0.95)	
No Insurance	1.10 (0.68, 1.77)		1.29 (1.04, 1.59)	

[a] Cumulative Incidence(CI) of Detection Risk Ratios: CI of Detection (group1) vs CI of Detection (Reference)
[b]CKD Stage was determined based on the abbreviated Modification of Diet in Renal Disease (MDRD) equation.

CHAPTER FIVE: IMPACT OF AUTOMATIC ESTIMATED GLOMERULAR FILTRATION REPORTING ON SCHEDULED NEPHROLOGY APPOINTMENTS AND KIDNEY FUNCTION IN A TERTIARY MEDICAL INSTITUTION

INTRODUCTION

Chronic kidney disease (CKD) affects more than one in ten Americans with an additional 20 million at risk. Approximately 13.1 % of the US non-institutionalized adult population is living with CKD.[1]. In the Medicare population, the prevalence of CKD has increased by over 200% from 1999 to 2009, 2.4% vs. 7.9%, respectively.

Once CKD is detected, treatments to delay the progression of kidney disease can be employed thereby reducing the patient morbidity and financial burden associated with end stage kidney disease (ESKD) management [24-27]. Nephrology referrals in the early disease stages also reduce the likelihood that patients will require emergency dialysis, and increase the likelihood of receiving standard renal therapy or a pre-dialysis transplant [44, 45]. Patients with CKD who are referred to nephrologists early have fewer complications and lower mortality rates than those who are referred late, [42] reducing the burden to the healthcare system. The 5-year survival rate for ESKD among those referred to nephrologists at least 6 months prior to dialysis is twice that of those who are referred later, less than 6 months prior to dialysis, (72.4% vs. 35.2%, respectively) [43].

To aid in identifying and managing kidney disease earlier, the National Kidney Foundation-Kidney Disease Outcome Quality Initiative (KDOQI) developed guidelines [52] that recommended estimated glomerular filtration rates (eGFR), based on the Modification of Diet in Renal Disease (MDRD) equation be reported concurrently with any serum creatinine (SCr) measurement. This recommendation eliminated the need for physicians to manually determine eGFR and thus help facilitate the early detection of CKD[52].

Many international and US-based healthcare organizations and laboratories implemented policies to automatically report eGFR when SCr is measured [31, 32, 37, 68, 69]. Although the utility [31, 32, 35, 38, 43, 52, 68, 70, 71] and role of automatic eGFR reporting remains unsettled, studies have shown that automatic eGFR reporting resulted in increased CKD detection, referrals, consults, and first time visits to nephrology clinics [34, 36-40, 68].

The aims of our study were to evaluate whether the implementation of automatic eGFR reporting increased scheduled nephrology appointments among patients with a low eGFR measurement compared to the period prior to automatic eGFR reporting and to examine patient characteristics related to scheduling of nephrology appointments. Few studies have had an opportunity to examine the impact automatic eGFR reporting has on eGFR levels as a result of scheduled nephrology appointments, while others report the paucity of data examining this patient outcome [38, 67, 72]. Our study also sought to evaluate changes in CKD function by automatic eGFR reporting periods among those with and without a scheduled nephrology appointment.

Methods

Automatic eGFR reporting:

The University of North Carolina Healthcare System (UNCHS) implemented a system-wide CKD initiative to automatically report eGFR (based on the MDRD equation), on all SCr tests ordered on adults 18 years or older in April 2005. Two memos were distributed and dissemination sessions were held to inform all physicians, and health care providers in the system of the new initiative.

Study Population

Patients in the UNCHS, ages 18-70 years old, with no previous history of kidney disease and who had at least one eGFR value less than 60 mL/min/1.73m2 from January 2004-December 2010 were included in this study (N=15,044). Patients with prior UNCHS nephrology clinic visits were excluded (N=204).

Data Source:

The patients' sex, race, comorbidities, and GFR levels were identified from the clinical medical records and laboratory information in the UNCHS WebClinical Information System (WebCIS). Information about scheduled nephrology appointments were obtained from the UNCHS appointment scheduling system. Patient's age at visit, diagnoses, and primary insurance coverage were obtained from the administrative billings claims data from Physicians and Associates, the billings organization that processes all claims for the UNCHS. All data were retrieved by the North Carolina Translational Science Institute Clinical Data Warehouse for

Health, a biomedical informatics resource that manages all UNCHS clinical and research data. The Institutional Review Board of The UNC School of Medicine, as well as the UNCHS Governance Board approved this study.

Measurements

The categorization of race/ethnicity included African American, White, and Other race (American Indian, Asian/Pacific Islander, Hawaiian, Hispanic, or Other race). The patient's age was determined as the number of years between birth date and clinic visit date. Morbidity was defined by at least one diagnosis code (International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)) in the medical record within one year prior to the date of the low eGFR measurement, and included diabetes mellitus (ICD-9-CM: 250, 250.5), essential hypertension (ICD-9-CM: 401 and 402), and cardiovascular disease (ICD-9-CM: 410-414,428,429.2,430-438). Initial kidney function levels were categorized using the stages of CKD (3:30-59 mL/min/1.73m^2; 4:15-29 mL/min/1.73m^2; 5:< 15 mL/min/1.73m^2).

Patient's health insurance was categorized as no insurance, private (Blue Cross/ Blue Shield, CHAMPUS, commercial insurance carriers and HMO/PPO), public (Medicaid, Medicare A or Medicare B), and a combination of both public and private insurance. Those lacking insurance information in the data source were categorized as missing insurance information.

The eGFR reporting period was defined as pre-initiative and post-initiative. Patients were categorized as pre-initiative if their first visit date was prior to April 2005. Conversely, patients with service dates after April 2005 were categorized as post-initiative.

Assessment of eGFR

Estimates of eGFR were identified in two ways. For patients whose service date occurred after April 2005 (post-initiative), the eGFR value was abstracted from WebCIS. For patients whose service date occurred before April 2005 (pre-initiative), the MDRD equation was used to calculate patients' eGFR, consistent with the method used by UNCHS' automated eGFR reporting via WebCIS.

Nephrology Scheduled Appointments and Visits

The UNCHS appointments scheduling database was searched to determine if an appointment was scheduled for the patient within one year following a low eGFR measurement. If no indication of an appointment was identified in the appointment scheduling system, the patient was classified as having no scheduled nephrology appointment.

Patient Outcomes via Change in CKD Function

Laboratory records were searched to identify follow-up SCr measurements within 12 months following the initial nephrology visit to determine eGFR and CKD stage, for those with a scheduled nephrology appointment. Similarly, laboratory records were also searched for SCr measurements within 12 months following the initial laboratory value, for patients who did not have a scheduled nephrology visit. Change in CKD function was determined as the difference between CKD stage at the last SCr measurement and the CKD stage at the initial SCr measurement. The change was categorized as 1) no change, 2) deterioration of kidney function and 3) improvement of kidney function. Those whose subsequent eGFR lab level is the same as the initial lab eGFR level are defined as No change; a deterioration of kidney function was

defined by the decrease in eGFR levels in the subsequent lab when compared to the initial lab. For example a reduction in eGFR from 15-29mL/min/1.73m^2 to <15mL/min/1.73m^2 would be categorized as a deterioration in function. Lastly, when the subsequent eGFR level was higher than the initial eGFR lab value the change is defined as an improvement of kidney function occurred. For example an individual whose initial lab value was 15-29mL.min/1.73m^2 and a subsequent lab value one year later was 30-59 mL/min/1.73m^2, would be categorized as an improvement in kidney function.

Statistical Analysis:

Summary statistics stratified by eGFR reporting period were obtained using basic descriptive analyses. The effect of automatic eGFR reporting on scheduled nephrology appointments was examined using multiple logistic regression. Characteristics associated with a scheduled nephrology appointment, after a low eGFR value, were identified by examining bivariate relationships between CKD detection and each covariate, overall and within subgroups. A nominal level of statistical significance of 0.05 was used to identify associations with covariates. Bivariate relationships between the outcome and each covariate, stratified by eGFR reporting period were used to determine patient characteristics associated with scheduled nephrologist appointments before and after reporting implementation. Within strata ordinal tests of association were conducted to examine associations between reporting period and changes in kidney function stratified by initial CKD stage. All analyses were conducted using SAS software (version 9.2, SAS Institute, Cary, NC).

Results

Baseline Characteristics

We identified 14,840 patients with an eGFR less than 60 mL/min/1.73m^2 Overall, 86.5% of the study population had an eGFR between 30-59 mL/min/1.73m^2, and approximately 7% had more severe kidney disease with an eGFR of $\leq$ 15 mL/min/1.73m^2. The majority of patients were women (57%), 30% were African American and 50% were aged 40-59 years. Approximately 87% percent had public, private or some combination of health insurance. Thirty-three percent of the patients had a history of hypertension, 14.6% a history of diabetes, 14.5% a history of CVD (Table 7). A total of 5,467 patients were identified pre-initiative, 9,373 were post-initiative.

Characteristics Associated With Scheduled Nephrology Visit

Only 15% of the study population (N=2,156) had a scheduled a nephrology appointment within one year in the UNCHS whereas 85% (N=12,684) did not have a scheduled appointment within one year in the UNCHS. A higher proportion of those with lower eGFR values had a scheduled a nephrology appointment compared to those with higher eGFR values (Stage 5 57%, Stage 4 32%, Stage 3 9.8%). (Table 7) Similarly, a higher proportion of African Americans had scheduled appointments compared to whites (20.1% vs. 11.9%). Younger patients and those who travel the furthest distance to UNCHS had higher proportions of scheduled appointments. Whereas the cohort of patients with both public and private health insurance had higher proportions of scheduled appointments compared to those with either insurance type or no insurance at all. (Table 7)

Characteristics Associated With Automatic eGFR Reporting and Scheduled Nephrology Visits

The proportion of patients with a low eGFR measurement who were scheduled for a nephrology appointment were similar for the pre-initiative period and post-initiative period of automatic eGFR reporting (14.9% pre-reporting vs. 14.3% post-reporting). Among those with scheduled appointments, 816 patients were identified during the period before automatic eGFR reporting and 1340 during the period after automatic eGFR reporting. (Table 8)

The proportion of scheduled visits was higher post eGFR reporting initiative then pre eGFR reporting among individuals with an eGFR level of <15mL/min/1.73m^2 (28.6% vs. 23.8 %), those aged 40-59 (50.0% vs. 55.9%) and those individuals with previous history of known risk factors for CKD (hypertension (14.8% vs. 29.4%); diabetes (8.9% vs. 15.4%); and CVD (6.1% vs. 10.1%). Conversely, individuals with eGFR between 15-29 mL/min/1.73m^2 and aged 25-39 (17.3% vs. 21.2%) had a lower proportion of scheduled appointments post eGFR reporting initiative compared to pre-eGFR reporting initiative. However, no differences in the proportion of scheduled visits pre reporting and post reporting were observed for sex, race, health insurance and health access (Table 8).

Individuals with eGFR levels between 15-29 mL/min/1.73m^2 and eGFR <15 mL/min/1.73m^2 were significantly more likely to schedule a nephrology visit pre-initiative than those with eGFR between 30-59 mL/min/1.73m^2 (OR=3.94; 95% CI: 3.17, 4.90; and OR=5.99; 95% CI: 4.87, 7.37 respectively). African Americans were 2.39 times as likely to have a scheduled nephrology visit as Whites (OR=2.39; 95%CI: 1.94, 2.94), and men were more likely

to have a scheduled nephrology visit than women pre-initiative (OR: 1.56; 95%CI: 1.34, 1.81). Individuals with hypertension were less likely to have a scheduled appointment pre-reporting initiative than those with no hypertension (OR= 0.73; 95% CI (0.54, 0.99). Similar results were observed for diabetes and CVD (diabetes (OR=1.01; 95% CI (0.78, 1.31); CVD (OR=0.78; 95%CI (0.63, 0.95). Similar factors were found to be independently associated with having a scheduled nephrology visit post-initiative; eGFR level, race, sex, CKD risk factors, and distance travelled to UNC. Those with an eGFR between 15-29 mL/min/1.73m^2 were 4.73 times more likely to be scheduled than those with eGFR between 30-59 mL/min/1.73m^2 (OR=4.73 95% CI: 3.89, 5.75). African Americans were 71% more likely to be scheduled post-initiative than those patients of other races (OR=1.71; 95% CI: 1.45, 2.02) as shown in Table 9.

Changes in eGFR Levels

Changes in eGFR levels were evaluated for those patients with subsequent SCr measurements 12 months after the initial nephrology visit (n=872) or 12 months after the initial low lab (n=3165, for those without a nephrology visit). Overall, nearly 50% had an improvement in kidney function, 6% had a deterioration of kidney function and 44% had no change in stage 12 months after their initial appointment or low lab (Data not shown).

When examining changes in eGFR levels among those who had a nephrology appointment, there was a significant change in the proportion of those who had an improvement in kidney function pre and post reporting initiative (p=0.011). Thirty-eight percent observed a decrease in stage after automatic eGFR reporting as compared to 30 % before automatic eGFR reporting. Fewer people experienced a worsening of disease (increase in CKD stage) after

implementation of eGFR reporting compared to before reporting (12.9% vs. 14.4% respectively – Table 10). There was a marginally significant increase in the proportion of people who had no change in the eGFR levels before eGFR reporting compared to after (p-value 0.05; 0.55 vs. 0.49, respectively – Table 10).

Similar trends were observed among those who did not have a scheduled nephrology appointment. Twelve months after the initial low SCr lab there were 3,165 individuals with subsequent SCr measurements. Forty-two percent of these patients had no change in their eGFR levels, 54% regained some level of function (increase in eGFR level) and 3.4% lost further function in their kidneys (decrease in eGFR level - Data not shown). The trends in changes in eGFR levels before and after eGFR reporting among those with no nephrology appointment were similar to those who had a nephrology appointment. However, there was a significantly higher proportion of people who had an increase in eGFR levels after automatic eGFR reporting than compared to before automatic eGFR reporting ($p<0.001$; 62% vs. 44%), a fewer proportion of people had a decrease in eGFR levels (2% vs. 5%) and no change in eGFR (35.9% vs. 50.9%). For each level of eGFR, there was a significant difference in the changes in eGFR levels pre and post automatic eGFR reporting, with the large majority of the individuals having an increase in eGFR levels post automatic eGFR reporting compared to pre reporting for each baseline level of eGFR.

The magnitude of the change in mean GFR levels was comparable before and after reporting. The values were also similar among those with and without a scheduled nephrology

appointment. One notable observation was that the range of mean changes was wider among those with no nephrology appointment compared to those with a scheduled. (Table 11)

Discussion

We evaluated the impact of the automatic eGFR reporting initiative in a tertiary healthcare center. No differences were observed in the proportion of new nephrology referrals for patients screened pre-initiative compared to post-initiative. Interestingly, the odds of obtaining a scheduled nephrology appointment were lower for individuals with known CKD risk factors, regardless of the eGFR reporting period than those without known risk factors. After implementation of eGFR reporting, the majority of individuals with a scheduled nephrology appointment showed no change in CKD stage for up to 12 months, or had an improvement in kidney function (decrease in CKD stage). This pattern was more pronounced in the post implementation phase of eGFR reporting. Post-implementation of eGFR reporting, the majority of those without a nephrology visit showed an improvement of kidney function in eGFR ensuing 12 months, not influenced by baseline level of eGFR. The evaluation of change in eGFR levels indicated minimal to no impact on kidney outcomes as a result of eGFR reporting.

Studies have reported conflicting results regarding the impact automatic eGFR reporting has on consults and referrals [37, 68, 73, 74]. A Canadian study of adult patients from a tertiary health care center found that there was an increase in the absolute number of referrals after eGFR reporting; however there was no increase in the proportion of referrals.[73] A US-based study of adults showed an increase in referrals for earlier stages of CKD but the increase was not sustained two years following the initiation of reporting[68]. Similarly a study from Ottawa

examined the ten-year impact of eGFR reporting using time series analysis and found a sudden but not sustained increase in nephrology consults [37]. Additionally a study evaluating the impact of eGFR reporting on the management of hospitalized patients in New York reported no increase in the number of nephrology consults[74]. We found an increase in nephrology referrals among those with eGFR levels <15mL/min/1.73m^2, those 40-59 years of age and those with no health insurance. However, we did not examine the sustained impacts of automatic eGFR reporting.

Our study suggests that patients who are at greater risk for CKD (those with diabetes, hypertension and/or CVD) have lower odds of a scheduled nephrology appointment regardless of reporting period. Additional analyses showed that there were low proportions of scheduled nephrology visits among patients with hypertension, diabetes and CVD after a low eGFR lab value was reported. While more than 90% of the patients with comorbidities had moderate eGFR levels 30-59 mL/min/1.73m^2, it is possible that physicians may decide to focus on intervening and controlling the comorbidities while monitoring the kidney function before a making a nephrology referral.

One argument used to support the implementation of automatic eGFR reporting included improving early detection of CKD in hopes of reducing the downstream burden of complications from late nephrology referrals. This argument has been tempered with the concern that automatic eGFR may lead to an increased number of unnecessary nephrology referrals, thereby overwhelming subspecialists and preventing access to nephrologists for individuals that truly require intervention [68, 71, 75, 76]. Moreover, one retrospective study showed that automatic

eGFR reporting increased nephrologists' workload but did not reduce the frequency of referral for those with severe kidney disease (stage 4 or 5). [71] The findings from our study do not support these concerns. There was no significant increase in scheduled nephrology appointments pre- or post-automatic eGFR reporting periods, although improvements in kidney function were observed in post- automatic eGFR reporting period. In fact, only 8% more individuals were found to have a significant improvement in their kidney function one year later post eGFR reporting compared to pre-eGFR reporting, among those scheduled for a nephrology visit. We were not able to elucidate whether these individuals improved because they were cases of acute kidney injury that would resolve without subspecialty intervention, or if these individuals improved directly because of the management that was elicited through nephrology care.

A sensitivity analysis was conducted to estimate eGFR change at one year change in GFR levels among those who had two low SCr levels. The trend of a higher proportion of individuals improving or experiencing no change in GFR was the same among those with and without nephrology appointments and by reporting period. Therefore, the patterns observed may not solely be due to acute kidney injury, but may be indicative of the fact that eGFR reporting had no discernible impact on kidney outcomes in this study.

To our knowledge, this is the first published study to address the characteristics and the long-term impact of individuals that have been referred for nephrology care after the implementation of automatic eGFR reporting in a healthcare system. The representative nature of the population is strength of our study. The UNCHS provides care for a racially and economically diverse population of patients, and this study is representative of both the general

population of NC and the general demographics of the patients cared for in the healthcare system. Strength is the utilization of a large sample of individuals within an US based tertiary care hospital system with a combination of laboratory and patient level data. While it is encouraging to see that minorities have a greater rate of nephrology visits as expected, women have a noticeably low number of referrals, a finding that deserves further exploration in other settings.

Our study limitations include the lack of individual chart reviews and the inability to identify whether therapeutic plans were prescribed to patients as a result of their nephrology visit. Further, the limited availability of records resulted in a shorter pre-eGFR reporting time period that was not optimal, may have been insufficient as a baseline to examine the changes that occurred in association with the introduction of automated reporting of eGFR in a complex, tertiary healthcare center. The use of ICD-9 codes may have resulted in misclassification of the comorbidities if they were not coded correctly; however, we do not expect any misclassification to be differential in this high-risk population. Lastly, it is not possible to capture follow-up nephrology visits by health care providers outside of the UNCHS. To the degree that this occurred it would have attenuated our estimates of the referrals for subspecialty nephrologists both prior to and after the introduction of the automated reporting of eGFR.

Overall, our study revealed no increased volume of referrals for subspecialty nephrologists following the implementation of automatic eGFR reporting in a tertiary health care center in the Southeast US. We submit that future studies should strive to provide longer follow-up of these

individuals to assess whether an impact on the proportion of individuals progressing to ESKD care is observed in the longer term.

Table 7-Characteristics of UNC Healthcare System Patients* with One Low estimated Glomerular Filtration (eGFR) Lab Value (Overall and by Scheduled Nephrology Appointment status)

Characteristics	*Overall N=(14,840)*	*No Nephrology Appointment (N=12,684)*	*Nephrology Appointment (N=2,156)*
	N (%)	*N (%)*	*N (%)*
eGFR level[†] 30-59 mL/min/1.73m^2	12,831 (86.5)	11,574(90.2)	1,257(9.8)
15-29 mL/min/1.73m^2	996 (6.7)	674(67.7)	322(32.3)
<15 mL/min/1.73m^2	1,013 (6.8)	436(43.0)	577(57.0)
Women	8,436 (56.8)	7,427(88.0)	1,009(12.0)
Men	6,404 (43.2)	5,257(82.1)	1,147(17.9)
African-Americans[‡]	4,387 (29.6)	3,505(79.9)	882(20.1)
Other race	1,215 (8.2)	1,037(85.3)	178(14.7)
Whites	9,238 (62.3)	8,142(88.1)	1,096(11.9)
Age: 18-24 years of age	241 (1.6)	149(61.8)	92(38.2)
25-39 years of age	1,527 (10.3)	1,122(73.5)	405(26.5)
40-59 years of age	7,392 (49.8)	6,235(84.3)	1,157(15.7)
60-70 years of age	5,680 (38.3)	5,178(91.2)	502(8.8)
Hypertension[§]	4,936 (33.3)	4,421(89.6)	515(10.4)
Diabetes[§]	2,164 (14.6)	1,884(87.1)	280(12.9)
Cardiovascular disease[§]	2,159 (14.5)	1,973(91.4)	186(8.6)
No Health Insurance**	1,554 (12.8)	1,360(87.5)	194(12.5)
Public Insurance	5,509 (45.5)	4,749(86.2)	760(13.8)
Private Insurance	3,748 (30.9)	3,160(84.3)	588(15.7)
Public & Private Insurance	1,301 (10.7)	1,062(81.6)	239(18.4)
Missing Health Insurance information	2,728	2,353	375
Miles traveled to UNC: Less than 20 miles[***]	5,849 (43.8)	5,363(91.7)	486(8.3)
20-49 miles	4,072 (30.5)	3,486(85.6)	586(14.4)
50-99 miles	2,358 (17.6)	1,873(79.4)	485(20.6)
More than 100 miles	1,089 (8.1)	831(76.3)	258(23.7)
Missing Distance	1,472	1,131	341

Characteristics	*Overall N=(14,840)*	*No Nephrology Appointment (N=12,684)*	*Nephrology Appointment (N=2,156)*
	N (%)	*N (%)*	*N (%)*
No Health Insurance**	1,554 (12.8)	1,360(87.5)	194(12.5)
Public Insurance	5,509 (45.5)	4,749(86.2)	760(13.8)
Private Insurance	3,748 (30.9)	3,160(84.3)	588(15.7)
Public & Private Insurance	1,301 (10.7)	1,062(81.6)	239(18.4)
Missing Health Insurance information	2,728	2,353	375
Miles traveled to UNC: Less than 20 miles***	5,849 (43.8)	5,363(91.7)	486(8.3)
20-49 miles	4,072 (30.5)	3,486(85.6)	586(14.4)
50-99 miles	2,358 (17.6)	1,873(79.4)	485(20.6)
More than 100 miles	1,089 (8.1)	831(76.3)	258(23.7)
Missing Distance	1,472	1,131	341

*All data were derived from UNC Healthcare System data for 2004-2010. The study population included patients with at least one SCr lab value <60 mL/min/1.73m2. Patients with unknown race, gender and age, and previous kidney disease were excluded. The Scheduled Nephrology Appointment status was determined whether or not an appointment was scheduled for the patient within one year following a low estimated Glomerular Filtration (eGFR) in the UNCHS.

† eGFR level was determined based on the abbreviated Modification of Diet in Renal Disease (MDRD) equation.

‡ Based on the race/ethnicity reported in medical record. 'Other' race includes all patients with race/ethnicity identified as American Indian, Asian/Pacific Islander, Hawaiian, or Other race.

§ Patients with comorbidities identified in medical records (via ICD-9 codes) at least once within one year prior to clinic visit were identified classified as having Hypertension (401,402); Diabetes (250, 250.5, and 250.5); CVD (410-414,428, 429.2, 430-438)

**Health insurance coverage was determined based upon the insurance that was identified in the medical records within 60 days of the visit. Private (Blue Cross, CHAMPUS, Commercial, HMO/PPO) Public (Medicaid, Medicare A, Medicare B), No Health Coverage (Self-Pay, Workers' Compensation) Data are missing for patients with unknown insurance.

***Miles traveled to UNCHS based upon the distance between UNCHS and patient address

Table 8-Characteristics of UNC Healthcare System Patients* with One Low estimated Glomerular Filtration (eGFR) Lab Value by Scheduled Nephrology Appointment status and eGFR Reporting Period

	Pre-Initiative Jan 2004- April 2005 *(N=5467)*		**Post-Initiative May 2005- Dec 2009** *(N=9,373)*	
Characteristic	*No Nephrology Appointment*	*Scheduled Appointment*	*No Nephrology Appointment*	*Scheduled Appointment*
	N (%)	*N (%)*	*N (%)*	*N (%)*
Overall	4,651 (85.1)	816 (14.9)	8,033 (85.7)	1.340 (14.3)
eGFR level† 30-59 mL/min/1.73m^2	4,059 (87.3)	476 (58.3)	7,515 (93.6)	781 (58.3)
15-29 mL/min/1.73m^2	316 (6.8)	146 (17.9)	358 (4.5)	176 (13.1)
<15 mL/min/1.73m^2	276 (5.9)	194 (23.8)	160 (2.0)	383 (28.6)
Women	2,719 (58.5)	387 (47.4)	4,708 (58.6)	622 (46.4)
Men	1,932 (41.5)	429 (52.6)	3,325 (41.4)	718 (53.6)
African-Americans‡	1,389 (29.9)	342 (41.9)	2,116 (26.3)	540 (40.3)
Other race	319 (6.9)	58 (7.1)	718 (8.9)	120 (9.0)
Whites	2,943 (63.3)	416 (51.0)	5,199 (64.7)	680 (50.7)
Age: 18-24 years of age	59 (1.3)	35 (4.3)	90 (1.1)	57 (4.3)
25-39 years of age	390 (8.4)	173 (21.2)	732 (9.1)	232 (17.3)
40-59 years of age	2,195 (47.2)	408 (50.0)	4,040 (50.3)	749 (55.9)
60-70 years of age	2,007 (43.2)	200 (24.5)	3,171 (39.5)	302 (22.5)
Hypertension§	853 (18.3)	121 (14.8)	3,568 (44.4)	394 (29.4)
Diabetes§	413 (8.9)	73 (8.9)	1,471 (18.3)	207 (15.4)
Cardiovascular disease§	383 (8.2)	50 (6.1)	1,590 (19.8)	136 (10.1)
No Health Insurance**	296 (11.6)	48 (9.3)	1,064 (13.7)	146 (11.5)
Public Insurance	1,146 (45.1)	224 (43.6)	3,603 (46.3)	536 (42.3)
Private Insurance	803 (31.6)	166 (32.3)	2,357 (30.3)	422 (33.3)
Public & Private Insurance	297 (11.7)	76 (14.8)	765 (9.8)	163 (12.9)
Missing Health Insurance information	2,109	302	244	73
Miles traveled to UNC: Less than 20 miles***	1,732 (44.0)	174 (26.2)	3,631 (47.7)	312 (27.1)
20-49 miles	1,192 (30.3)	205 (30.8)	2,294 (30.1)	381 (33.1)
50-99 miles	721 (18.3)	189 (28.4)	1,152 (15.1)	296 (25.7)
More than 100 miles	295 (7.5)	97 (14.6)	536 (7.0)	161 (14.0)
Missing Distance	711	151	420	190

*All data were derived from UNC Healthcare System data for 2004-2010. The study population included patients with at least one SCr lab value <60 mL/min/1.73m2. Patients with unknown race, gender and age, and previous kidney disease were excluded. The Scheduled Nephrology Appointment status was determined whether or not an appointment was scheduled for the patient within one year following a low estimated Glomerular Filtration (eGFR) in the UNCHS. . The eGFR reporting period was determined by the timing of the patient visit relative to the implementation of the automatic eGFR reporting initiative in the UNCHS before April 2005 (Pre-); after April 2005 (Post-).

† eGFR level was determined based on the abbreviated Modification of Diet in Renal Disease (MDRD) equation.

‡ Based on the race/ethnicity reported in medical record. 'Other' race includes all patients with race/ethnicity identified as American Indian, Asian/Pacific Islander, Hawaiian, or Other race.

§ Patients with comorbidities identified in medical records (via ICD-9 codes) at least once within one year prior to clinic visit were identified classified as having Hypertension (401,402); Diabetes (250, 250.5, and 250.5); CVD (410-414,428, 429.2, 430-438)

**Health insurance coverage was determined based upon the insurance that was identified in the medical records within 60 days of the visit. Private (Blue Cross, CHAMPUS, Commercial, HMO/PPO) Public (Medicaid, Medicare A, Medicare B), No Health Coverage (Self-Pay, Workers' Compensation) Data are missing for patients with unknown insurance.

***Miles traveled to UNCHS based upon the distance between UNCHS and patient address

Table 9- Factors Associated with a Scheduled Nephrology Visit by eGFR reporting Period

	Overall	Pre-Initiative Jan2004-April 2005 *Odds of having a scheduled nephrology appointment Ratio (95% CI)*	Post-Initiative May 2005-Dec 2009 *Odds of having a scheduled nephrology appointment Ratio (95% CI)*
eGFR level[b]			
30-59 mL/min/1.73m^2	12,831 (86.5)	Ref.	Ref.
15-29 mL/min/1.73m^2	996 (6.7)	3.94(3.17,4.90)	4.73(3.89,5.75)
<15 mL/min/1.73m^2	1,013 (6.8)	5.99(4.87,7.37)	23.03(18.88,28.09)
Age: 18-24	241 (1.6)	3.19(2.07,4.91)	3.42(2.43,4.80)
25-39	1,527 (10.3)	2.39(1.94,2.94)	1.71(1.45,2.02)
40-59	7,392 (49.8)	Ref.	Ref.
60-70	5,680 (38.3)	0.54(0.45,0.64)	0.51(0.45,0.59)
White race	241 (1.6)	3.19(2.07,4.91)	3.42(2.43,4.80)
African American race	1,527 (10.3)	2.39(1.94,2.94)	1.71(1.45,2.02)
Other race	7,392 (49.8)	Ref.	Ref.
Women	8,436 (56.8)	Ref.	Ref.
Men	6,404 (43.2)	1.56(1.34,1.81)	1.63(1.46,1.84)
No History of CVD	12,681 (85.5)	Ref.	Ref.
History of CVD	2,159 (14.5)	0.73(0.54,0.99)	0.46(0.38,0.55)
No History of Diabetes	12,676 (85.4)	Ref.	12,676 (85.4)
History of Diabetes	2,164 (14.6)	1.01(0.78,1.31)	0.82(0.70,0.96)
No History of Hypertension	9904 (66.7)	Ref.	Ref.
History of Hypertension	4,936 (33.3)	0.78(0.63,0.95)	0.52(0.46,0.59)
Miles traveled to UNC: Less than 20 miles	5,849 (43.8)	Ref.	Ref.
Traveled 20 to 49 miles	4,072 (30.5)	1.71(1.38,2.12)	1.93(1.65,2.26)
Traveled 50 to 99 miles	2,358 (17.6)	2.61(2.09,3.26)	2.99(2.52,3.55)
Traveled more than 100 miles	1,089 (8.1)	3.27(2.48,4.32)	3.50(2.83,4.32)
No insurance	1,554 (12.8)	Ref.	Ref.
Private insurance only	5,509 (45.5)	1.21(0.86,1.69)	1.08(0.89,1.32)
Public Insurance only	3,748 (30.9)	1.27(0.90,1.80)	1.30(1.07,1.60)
Public and Private insurance	1,301 (10.7)	1.58(1.06,2.34)	1.55(1.22,1.98)

[a] Odds of Scheduled Nephrology Appointment Ratios: Odds of having a Scheduled Nephrology Appointment (group1) vs. Odds of No scheduled Appointment (Reference)

1

Table 10- One year Within Patient Changes in eGFR Levels by Scheduled Nephrology Appointment Status

	Had a Scheduled Nephrology Appointment (N=872)			No Nephrology Appointment (N=3165)		
	Before eGFR reporting (N=416)	After eGFR reporting (N=456)	p-value	Before eGFR reporting (N=1369)	After eGFR reporting (N=1796)	p-value
Overall						
Decrease in CKD Stage[1]	125(30.0)	174(38.2)	0.011	602(44.0)	1,113(62.0)	<0.001
No Change[2]	231(55.5)	223(48.9)	0.050	697(50.9)	645(35.9)	<0.001
Increase in CKD Stage[3]	60(14.4)	59(12.9)	0.524	70(5.1)	38(2.1)	<0.001

[1]Decrease in CKD Stage is change in GFR level equivalent to a CKD stage lower than initial GFR level
[2]No Change in CKD Stage is where initial GFR levels are equivalent to subsequent GFR levels.
[3]Increase in CKD Stage is change in GFR level equivalent to a CKD stage higher than the initial GFR level

Table 11-Mean GFR Level One-year Within Patient Change by Scheduled Nephrology Appointment Status and Change in CKD Stage[1]

	Had a Scheduled Nephrology Appointment (N=872)				No Nephrology Appointment (N=3165)			
	Before eGFR reporting (N=416)		After eGFR reporting (N=456)		Before eGFR reporting (N=1369)		After eGFR reporting (N=1796)	
	Mean GFR Change (Std Dev)	Range	Mean GFR Change (Std Dev)	Range	Mean GFR Change (Std Dev)	Range	Mean GFR Change (Std Dev)	Range
Decrease in CKD Stage[1]	29.21 (21.86)	116.59	32.22 (24.44)	132.49	24.57 (19.75)	142.36	28.88 (25.84)	222.94
Increase in CKD Stage[2]	-17.42 (11.32)	48.03	-20.32 (11.56)	47.05	-18.84 (10.56)	51.92	-19.46 (12.19)	55.10
No Change[3]	-1.05 (6.92)	41.24	-1.62 (8.01)	46.75	-0.87 (7.82)	55.17	-0.65 (8.80)	56.85

[1]Decrease in CKD Stage is change in GFR level equivalent to a CKD stage lower than initial GFR level
[2]Increase in CKD Stage is change in GFR level equivalent to a CKD stage higher than the initial GFR level
[3]No Change in CKD Stage is where initial GFR levels are equivalent to subsequent GFR levels.

CHAPTER SIX: DISCUSSION

Study Rationale

Several studies reported an increasing temporal trend in frequency of occurrence of CKD, [1-4] with the prevalence of CKD ranging from 3% to 30 %. [5-11]. CKD and ESKD lower patient quality of life, cause premature morbidity and mortality, and lead to economic burden on individuals, health care systems and society.[12] Early diagnosis and management of kidney disease on the other hand can delay the progression to ESKD and avert the cardiovascular sequelae associated with CKD [13, 14]. Despite the high population burden of CKD, awareness and detection of kidney disease in the US is low among consumers and providers of healthcare services. [3, 15-19]. Furthermore, despite knowledge that early detection and medical management are key to slowing the progression of kidney disease, delayed referrals to nephrologists are common.

Automatic eGFR reporting initiatives were implemented by international and US-based healthcare organizations and clinical laboratories to increase reporting efficiency, facilitate the early diagnosis of Chronic Kidney Disease (CKD), and improve early medical management to minimize CKD burden. International population studies have shown that automatic eGFR reporting resulted in increased CKD detection, referrals, consults, and first time visits to

nephrology clinics [20-24]. In contrast, the impact of eGFR reporting in US healthcare systems remains unclear [25-27].

Specific Aims

This study sought to assess whether automatic eGFR reporting has a measurable effect on CKD detection and patient care, and to identify patient characteristics related to benefit from eGFR reporting in terms of detection and referral. To achieve this goal we addressed the following aims:

Specific Aim 1: To quantify the detection of CKD detection prior to and following the implementation of automatic eGFR reporting among adults patients *who had at least one SCr measurement with an eGFR measurement below 60ml/min/1.73m^2* seen in the UNC Healthcare System (UNCHS) between January 2004 and December 2010.

Specific Aim 2: To quantify the proportion of adults who *had a second SCr measurement after an initial eGFR <60 ml/min/1.73m^2* before and after the implementation of automatic eGFR reporting seen in the UNC Healthcare System (UNCHS) between January 2004 and December 2009.

Specific Aim 3: To quantify the detection of clinically identified CKD before and after the implementation of automatic eGFR reporting among adult patients with lab-verified moderate to severe CKD (i.e. *two eGFR measurements below 60ml/min/1.73m^2)* seen in the UNC Healthcare System (UNCHS) between January 2004 and August 2009.

Specific Aim 4 : To examine the proportion of nephrology referrals to UNC Nephrology clinics for adult patients with stage 3 CKD or higher before and after the implementation of automatic eGFR reporting in the UNCHS

Summary of Findings

To examine the impact of the eGFR reporting initiative on CKD detection in a tertiary care health care institution we estimated 1-year cumulative incidence (CI) and difference (CID) of CKD detection in the study cohort pre- and post-initiative. Patient characteristics associated with CKD detection were then assessed, overall and by reporting period.

Following the introduction of automatic eGFR reporting, CKD detection increased by 9%, with a greater increase in detection found among those with moderate CKD (Stage III, eGFR: 30-59 mL/min/1.73m^2). The increase in CKD detection post eGFR reporting initiative, was greatest in older adults, males, whites and those with a history of hypertension, diabetes and CVD. Although a moderate increase in CKD detection was observed overall, the greatest increase was in the second year of implementation, and the increase was not sustained in subsequent years.

Prior to the reporting initiative the following factors were statistically independently associated with CKD detection: eGFR level, age, race and gender. Factors that we found to be independently associated with CKD detection post-initiative were eGFR level, race, and comorbidities. Those with lower eGFR levels (15-29 mL/min/1.73m^2) were almost 2 times as likely to be detected as those with eGFR levels between 30-59 mL/min/1.73m^2. Following implementation of the eGFR reporting initiative, CKD was more likely to be detected among

African Americans than in whites and among those with a history of CVD, hypertension and diabetes than those without the comorbidity.

We found that the overall CKD detection rates were low in this patient population, despite the broad education efforts that made to increase CKD awareness within the institution and North Carolina. Although surprising for this institution, similar results have been reported by others.[6, 27, 40]

We also sought to examine whether the introduction of the automatic eGFR reporting initiative was associated with the number of scheduled nephrology appointments, to identify the patient characteristics associated with scheduling nephrology appointments, and to evaluate a potential impact of automated eGFR reporting on the temporal trends in patient's kidney function among those with and without a scheduled nephrology appointment. No increase in the number of referrals for subspecialty nephrologists following the implementation of automatic eGFR reporting was observed, which represents an important finding since it does not support the generally held expectation that eGFR reporting increases the workload for nephrologists.

Additionally, we observed that the odds of obtaining a scheduled nephrology appointment were lower for individuals with known CKD risk factors (hypertension, CVD, and diabetes), regardless of the eGFR reporting period. We further observed that following implementation of eGFR reporting, the majority of patients with a scheduled nephrology appointment showed no change in CKD stage at one year after the appointment, or experienced an improvement in kidney function (decrease in CKD stage). This pattern was more pronounced

in the post-initiative phase of eGFR reporting. Post-implementation of the eGFR reporting initiative, the majority of those without a nephrology visit showed an improvement of kidney function in eGFR during the ensuing 12 months, not influenced by baseline level of eGFR. The evaluation of change in eGFR levels indicated minimal to no impact on kidney outcomes as a result of eGFR reporting, findings which were contrary to a priori expectations. Although we are unable to infer a cause for these findings we propose that the improvement could be indicative of acute kidney injury cases that would have resolved without subspecialty intervention.

In summary, this dissertation sought to evaluate the impact of automatic eGFR reporting within UNCHS. We found a slight non-significant increase in CKD detection as a result eGFR reporting but no increase in nephrology referrals or significant changes in kidney function at one year of follow-up. We conclude that automatic eGFR reporting had no discernible association with CKD detection or patterns of patient care with the UNC Health System.

Strengths and Limitations

This study utilized a large sample of individuals within an US based tertiary care hospital system with a combination of laboratory and patient level data to explore the study objectives. Several logistical, operational and methodological challenges were encountered in conducting this research. Data availability emerged as a significant challenge in this study. UNCHS data was only available from 2004-2010, which only included 15 months prior to the implementation of the eGFR reporting initiative for this study. The short timeframe for pre-eGFR reporting initiative may have been insufficient to examine the true association of detection and could lead

to misclassification of comorbidities and patient characteristics. To address this limitation, the timeframe for identification of comorbidities and patient characteristics was limited to one year prior to the clinic visit date associated with the second low eGFR measurement, pre- and post-initiative, to minimize differential misclassification with respect to eGFR reporting period.

An operational as well as methodological challenge for this study derived UNCHS' status of referral center. As a result it is possible that patients had a second low eGFR measurement at an ambulatory center outside of UNHCS and therefore have a diagnosis of CKD prior to documentation at UNCHS of a second low eGFR. A sensitivity analysis was conducted to examine the risk of CKD detection among patients after their first low eGFR value. Results from the sensitivity analyses indicated similar detection patterns as those in the overall study, with a lower CKD detection post-initiative reporting, than pre- initiative reporting. The detection rates among this group did not differ with respect to magnitude or direction. Thus, selection bias due to the definition of lab-verified CKD should not significantly alter these results. The referral center status of UNCHS could also make it difficult to capture follow-up nephrology visits by health care providers outside of the UNCHS. To the degree that this occurred it would have attenuated our estimates of the referrals for subspecialty nephrologists both prior to and after the introduction of the automated reporting of eGFR.

A further concern is potential misclassification. Current CKD guidelines define CKD as persistent kidney dysfunction with or without the presence of kidney damage. This study could only assess kidney dysfunction through serum creatinine measures and not the presence of protein in a patient's urine. Patients with kidney damage who would be identified clinically as

having CKD were not identified in our study. The use of ICD-9 codes alone may have resulted in misclassification of the comorbidities if they were not coded correctly; however, we do not expect any misclassification to be differential in this high-risk population.

This study used electronic health records (EHR) as the main data source. EHR proved to be a rich source of data for this study and for many other research studies. However the use of EHR was also translated into an operational limitation. EHR data are generally not captured for research purposes and many key definitions and decisions must be made to utilize the data to answer research questions. With the advent of the Health Insurance Portability and Accountability Act that requires all health organizations (large and small) to implement the use electronic health records, there has been an increase in the use of EHR for research purposes because it minimizes the need to collect study data by using data that was already collected. However, caution should be exercised when studies use EHR for research purposes since careful attention to study definitions and study designs is required to ensure data quality. Much time and attention to detail was required to arrive at an appropriate study design and definitions for this study, and to ensure that the data were valid and with minimal opportunities for bias.

This study also had several strengths, one of which the examination of the characteristics and long-term impact of individuals that have been referred for nephrology care after the implementation of automatic eGFR reporting in a healthcare system; to our knowledge, this is the first study. The nature of the patient population is another strength of this study in that UNCHS provides care for a racially and economically diverse population of patients drawn from a wide geographic area that includes urban and rural sectors. These features favor the

generalizability of these findings as regards the patient population, although our results are seen as most applicable to tertiary health care settings. .

Public Health Impact

Although our results indicate that introduction of automated eGFR reporting in the UNCHS was not associated with a significant temporal increase in CKD detection and pattern of specialty care by nephrology, the study offers some insights on the factors that may deserve attention in order to achieve the desired impact of eGFR reporting. Based on our results and the overall low CKD detection rates observed we conclude that a more visible and sustained educational effort is likely required to increase awareness among patients and health care professionals of a system-wide eGFR reporting, its information value, and its actionable features. Such a campaign would likely benefit from information about CKD and the importance of CKD detection. Further, given that we observed no increase in the workload of nephrologists but did identify a temporal trend of kidney function improvement following the introduction of eGFR reporting, replication of these results in other health care settings and institutions that implement eGFR reporting is recommended to achieve clarity on the anticipated – but undocumented – greater engagement of nephrology specialist care resources as a result of automatic eGFR reporting. Lastly, based on our experience in this study we submit that electronic health records can be an asset as a resource for clinical research, although at cost of great attention to data completeness and data quality concerns, and reliance on detailed data management and research protocols.

As CKD continues to be a public health issue worldwide and the costs associated to treat those who are in the final stages of CKD continue to rise, it is of particular interest to explore avenues for early detection that enables early medical management and therapeutic interventions. Similarly, the identification of patient characteristics associated with detection and referral practices (e.g. SES, health care access, gender, insurance status, etc.) is of interest if it allows investigators to conduct targeted approaches to identify those individuals who may not be regularly screened or have a delay in referrals resulting in more severe and irreversible disease. A systematic approach such as automatic eGFR reporting broadens the scope of the detection efforts well beyond targeted screenings, although thus far it is mostly applied to selected patient populations. Far from being representative of the general population, the majority of patients seen in a tertiary care referral system represent a population enriched with morbidities and thus also their antecedent risk factors. The rationale for automatic reporting of eGFR in high risk populations such as most of the patients seen in the UNCHS is for earlier identification of those with kidney disease among them, to achieve earlier interventions to reduce progression of the disease to the end stages, and its burden of morbidity, mortality and economic drain.

Future Directions

We submit that further study to explore the effects attributed to automatic eGFR reporting policies on CKD detection and patient kidney function outcomes are warranted. Follow-up studies are encouraged given the need for sufficiently long pre- and post-initiative follow-up periods, as required to assess clinically meaningful and public health relevant effects that can be attributed to eGFR. The operational definition of CKD for such studies should include the characterization of kidney damage through the presence of proteinuria, to provide a more

complete picture of the putative benefits from an automatic eGFR reporting policy. Also based on the experience in this study we submit that more precise measures of nephrology referral deserve to be considered to advance our knowledge in this field.

APPENDIX 1: DESCRIPTION OF NCTRACS DATA SOURCE GUIDE

Files Received from NC TRACS

Dataset name	Dataset patient identifiers	Description of dataset	Data Structure and Development
DX1.xls- DX17.xls	patient_sk account_sk eff_date	Contains all diagnosis identified for patients in UNCHS	There is more than one DX for a given visit date. Restructured to include all identified diagnoses per patient per date on one observation.
Postalcode1.xls-Postalcode17.xls	patient_sk account_sk update_ts	Contains information on the billing addresses for patients. The update_ts variable indicates the date the address was updated in the system.	There were more than one observation for a given patient at times. The address that indicates the location the patient lived at during the identified clinic visits.
Demog1.xls-Demog17.xls	patient_sk medical_record_number	Contains the race, dob, gender of patients in UNCHS	Only one observation for each patient_sk
Echart1.xls-echart17.xls	patient_sk account_sk echartdate	Contains the height and weight of UNCHS patients	Admis_wt, echart_et and echartht are on separate observations for a given date Restructured to capture the height and weight for each patient on the same clinic visit date.
Lab1.xls-Lab17.xls	patient_sk lab1date	Contains the lab information for the flagged GFR labs	There was more than one observation for a given date, but that date corresponds to another lab pair indicated by pat_labid.

Dataset name	Dataset patient identifiers	Description of dataset	Data Structure and Development
Outpatientvisits1.xls-Outpatientvisits17.xls	patient_sk account_sk patient_visit_date	identifies the clinic the patient was seen in during the UNCHS visit	There were multiple clinic listings on a visit date. Restructured to capture all clinic visits on the same date for each patient.
Payor1.xls-Payor17.xls	patient_sk account_sk payor_date	Identifies the billing payor for the UNCHS visit	Only one observation for each patient_sk and payor_date
Problems1.xls-Problems17.xls	patient_sk account_sk problem_onset_date	identifies any comorbidities the patient had in medical record	There was more than one observation for a given date. Restructured to include all identified problems per patient per date on an observation.
Visits1.xls-Visits17.xls	patient_sk account_sk admission_date	identifies the inpatient admission information for the corresponding UNCHS visit	There is only one clinic information for each admission date.
Vitals1.xls-Vitals17.xls	patient_sk account_sk vital_date	Corresponds to height and weight for a UNCHS visit	There is only one weight and height for each visit (Never able to determine units so this was not used)
SKMRNList	patient_sk	Crosswalk table between patient SKs and their actual medical record numbers	There is only one record per person.

Dataset name	Dataset patient identifiers	Description of dataset	Data Structure and Development
NephAppts	Patient MRN	Appointment scheduler data for Nephrology clinic appointments earlier than 12/31/2010	There is only one record per person.
NephVisits	patient_sk	Hospital billing data for Nephrology clinic visits earlier than 12/31/2010	There is only one record per person.
NephVisitInsurers	patient_sk	Patients' insurance data for Nephrology clinic visits earlier than 12/31/2010	There is only one record per person.

APPENDIX 2: CLINICAL AND PROVIDER DATA SOURCE SUMMARY

	Description	How variable was categorized	Data Source	NCTRACS Source	Notes
Characteristics					
Demographics					
Patient Information					
Patient_sk	NCTracs unique patient identifier		All datasets from NCTRACs		
Medical Record Number	Unique identifier for patients seen in UNCHS		WEBCIS/ Accounting	Demog.xls	
Residence Billing Zip code			WEBCIS/ Accounting	Addresses.xls	
Inpatient indicator	Identified is patient was seen in an inpatient clinic		Accounting	Visits.xls	
Outpatient indicator	Identified is patient was seen in an Outpatient clinic		Accounting	Outpatients.xls	
Diagnosis codes	Will be used to determined indication of CKD diagnosis and other co morbidities.		WEBCIS & UNC P&A	DX	
Nephrology visit type	Will be used to determine if patient was seen in a nephrology clinic within one year of CKD diagnosis	1=New, 2=Consult, 3=return	UNC P &A	Visits	

	Description	How variable was categorized	Data Source	NCTRACS Source	Notes
Age via Date of birth	Patient's age at clinic visit	Continuous 18-39 40-59 60-69	WEBCIS/ Accounting	Demographics,	
Sex	Patient's sex	0=Male 1= Female	WEBCIS/ Accounting	Demog	
Race	Patient's race/ ethnicity	0=White 1=African American 2=Other	WEBCIS/ Accounting	Demog	
Health Insurance	Patient's type of insurance	0= No Insurance 1= Public 2=Private 3=Public and Private 4=Missing Health Insurance information	WEBCIS/ Accounting	Payor	
Weight	Patient's weight (kg)	Continuous	WEBCIS/ E-chart	Vitals and echart	This information was not used. NCTraCS could not clarify the unit types for the data.
Height	Patient's height (m)	Continuous	WEBCIS/ E-chart	Vitals and echart	This information was not used. NCTraCS could not clarify the unit types for the data.

	Description	How variable was categorized	Data Source	NCTRACS Source	
Patient's Residence	The billing zip code of the patient		WEBCIS/ Accounting	Addresses	This variable was used to determine distance from UNCHS
Hypertension	Has diagnosis of hypertension indicated with an ICD-9 code (401, 401.1, 401.1, 401.9, 402, 403, or 404)	0= Normotensive 1= Hypertensive	Accounting	Problems and DX	
Diabetes	Has diagnosis of diabetes indicated with an ICD-9 code (250, 250.4, 250.5, 362.01, or 362.02)	0= Non-diabetic 1= Diabetic	Accounting	Problems and DX	
CHD	Has diagnosis of CHD indicated with an ICD-9 (410 to 414, 429.2)			Problems and DX	
CVA	Has diagnosis of CVA indicated with an ICD-9 code (430 to 438)		Accounting	Problems and DX	
Heart Failure	Has diagnosis of HF indicated with an ICD-9 code (428)			Problems and DX	
MI	Has diagnosis of AMI indicated with an ICD-9 code (410)		Accounting	Problems and DX	
Obesity	Calculated using the height and weight obtained from charts	0= Normal 1=Obese	WEBCIS	Calculated	No calculated because weight and height could not be verified

	Description	How variable was categorized	Data Source	NCTRACS Source	
Laboratory Results					
Serum Creatinine	Reported from metabolic chemistry 7 or 10 panels.		Labs/ WEBCIS	Labs	
Estimated glomerular filtration rate (eGFR)	The estimated value using the MDRD equation.	Continuous	Labs/ WEBCIS	Labs	Calculated for the values before April 2005 and the reported value for those after April 2005.
Provider information					
Date of Service	The date of the clinic visit.		WEBCIS	Labs	
Scheduled Appointment	Indicator that identifies whether or not a patient has a scheduled Nephrology appointment		Accounting	Nephvisits and NephApts	
Change in Kidney Function	This indicates the changes in the eGFR levels from initial to subsequent eGFR	1= Decrease in function 0= No Change 2= Improvement in kidney function	Labs	Labs	Calculated from the difference between initial eGFR reading and subsequent eGFR reading

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