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Rania Jabi Date

Improving Outcome of Dialysis Patients in the Initiation Phase

By

Rania Jabi

Degree to be awarded:
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Executive Master of Public Health

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Improving Outcome of Dialysis Patients in the Initiation Phase

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MD

University of Damascus Faculty of Medicine

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A thesis submitted to the Faculty of the
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in partial fulfillment of the requirements for the degree of
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Abstract

Improving Outcome of Dialysis Patients in the Initiation Phase

By

Rania Jabi

Purpose: The purpose of this thesis was to refine general public health and practitioner knowledge regarding interventions that would improve dialysis patient outcomes including patient survival and quality of life. Patient morbidity and mortality could be reduced by systematically identifying measures that might improve dialysis outcomes. A systematic literature review would help reveal and evolve practices in this area.

Methods: This thesis utilized a systematic literature review with relevant articles and analyzed the data available to address the question of how to improve outcome of dialysis patients in the first year of dialysis treatment. The first year of dialysis is usually associated with high mortality, morbidity and healthcare cost. The systematic literature review produced ten peer reviewed studies for analysis. The common outcome variables in all studies were identified and compared.

Results: All of the selected studies contained important conclusions regarding the importance of vascular access type, arteriovenous fistula (AVF) and its benefits to improve patient outcome. Improving vascular access for incident hemodialysis patients was very important. This could be achieved by increasing the percentage of hemodialysis patients who use AVF as the primary mode of vascular access at the start of treatment.

Conclusions: Public Health and practitioner education is needed to increase the knowledge regarding the benefits of early referral of patients with advanced chronic kidney disease to nephrologist. This was also essential to improve outcome by providing better dialysis preparation and early placement of AVF. Providing structured programs for prompt educational and medical strategies in early end stage renal disease patients was promising and had potential benefits. Standardization of research data is needed as is additional research specifically including cost data.

THESIS

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Chapter 1: Introduction

Introduction and Rationale

Worldwide and especially in the United States, about 30 million US adults are estimated to have Chronic Kidney Disease (CKD) with the majority being undiagnosed. About 340 people begin dialysis treatment for kidney failure every day (CDC, 2018).

Mortality risk for dialysis patients is highest in the first year after starting dialysis (Wingard, Chan, Lazarus, & Hakim, 2009). In addition, poor planning for dialysis initiation may lead to catheter use and is associated with high infections. This will have a negative effect on patient survival during the first year following dialysis initiation (Collins, Foley, Gilbertson, & Chen, 2009). Therefore, contributing to higher morbidity rate and increased health care cost.

Morbidity and mortality risk are affected by the type of vascular access used at the beginning of dialysis (Lok & Foley, 2013). Public health programs, such as the new Medicare chronic kidney disease education benefit, are necessary to educate patients needing dialysis to reduce their high morbidity and mortality risk in the first year (Collins et al., 2009).

The purpose of this thesis is to update and inform general public health and practitioner knowledge regarding interventions that improve dialysis patient outcomes including patient survival and quality of life. Patient morbidity and mortality may be reduced by systematically identifying measures that improve public health practitioner knowledge and dialysis outcomes. A systematic literature review may help reveal and evolve practices in this area.

Problem Statement

Chronic Kidney disease (CKD) is increasingly recognized as a "major public health problem that requires a Public Health Action Plan" (Schoolwerth et al., 2006). More public health knowledge and information is needed so that both patients and clinicians have better and earlier knowledge regarding CKD progression and the information that could provide for better outcomes. CKD can lead eventually to end-stage renal disease (ESRD) and need for dialysis. The latter is associated with very high mortality and mobility as well as high healthcare cost especially during the first year after initiating dialysis.

There is a need to systematically apply informatics principles and data analysis to review existing studies to identify the most effective practice outcomes. New clinical practices leveraging technology such as Electronic Health Record tools and mobile phone apps can help in bridging this gap and reaching these favorable outcome goals (FMC, 2019).

US Experience Poor:

Despite some clinical initiatives such as Fistula First Initiative (FFI), to improve arteriovenous fistula (AVF) rate and therefore patient outcome, AVF rate remains significantly lower than that of other industrialized nations. It has been acknowledged that there are notable differences in dialysis between Japan and the United States. In Japan, AVF usage is high at (91%) and central venous catheter (CVC) usage is low at (1% to 2%). With this high mortality risk in U.S. hemodialysis patients as compared to Japanese patients, patients in Japan show better survival rates as compared to patients worldwide (Ozeki et al., 2017).

In the United States adult population, the overall prevalence of all stages of CKD was 14.8% in 2011-2014. The most prevalent was stage 3 CKD at (6.6%) (USRDS, 2017a). CKD is a serious clinical condition that could progress eventually to end-stage renal disease (ESRD) which would then require lifelong dialysis or kidney transplant. Forty percent of CKD individuals have diabetes (DM). In addition, 40% have cardiovascular disease and 32% have hypertension (HTN). (USRDS, 2017a).

Unlike other diseases, CKD is a subtle disease and many patients who have the disease are not aware of it. In a large representative telephone-based survey, the prevalence of self-reported CKD was very low in the U.S. population. The numbers ranged from 1.8% in Virginia to 4.0% in Arizona. These numbers are compatible with limited awareness of CKD among the 14% of the U.S. population who have this medical condition (USRDS, 2017a).

Once a patient is diagnosed with end-stage renal disease in the U.S., patient treatment options include dialysis (hemodialysis or peritoneal dialysis) or kidney transplant. The first months of dialysis are considered a critical period in the life of an end-stage renal disease patient. During this time, the patient becomes dependent on medical technology that can have a major role in his or her quality and life expectancy. The mortality rate of new dialysis patients after initiation of dialysis is very high. Previous registry data from Europe and North America showed that approximately 35% of the mortality during the first year of dialysis occurred in the first 90 days (Noordzij & Jager, 2014).

According to the latest U.S. Renal Data System Annual Data Report, more than 660,000 Americans are treated for end stage renal disease, or ESRD. Of these

individuals, 468,000 are dialysis patients and 193,000 have a functioning kidney transplant (National Kidney Foundation, 2017b). Medicare spending on both CKD and ESRD was over $98 billion in 2015. With costs exceeding $64 billion for beneficiaries who had chronic kidney disease (CKD; 11% of total) in addition to $34 billion for individuals with end-stage renal disease (ESRD) (USRDS, 2017g).

High U. S. Mortality Rates:

Mortality rate for Medicare patients with CKD was at 109.7 per 1,000 patient-years in 2015 as compared to the mortality rate of 45.6 per 1,000 patient-years of those without CKD after adjustment for age, race, and sex. These mortality rates increased with CKD severity, although the gap has narrowed between CKD and non-CKD patients from 2003-2015 (USRDS, 2017c).

Rehospitalization rate for CKD patients was at 21.5%. This was much higher than the 15.5% for those without CKD. In the Medicare patient population without CKD, males experienced a higher rehospitalization rate than did females, with age and race adjusted percentages of 16.2 and 14.9 (USRDS, 2017c).

There were 124,114 newly reported (incident) cases of ESRD in 2015 with the unadjusted (crude) incidence rate at 378 per million population. Both of these numbers have risen since 2011. The adjusted ESRD incidence rate ratios for Native Hawaiians/Pacific Islanders, Blacks/African Americans, American Indians/Alaska Natives, and Asians as compared with Whites were 8.4, 3.0, 1.2, and 1.0 in 2015. As compared to incidence, the number of ESRD prevalent cases continued to rise by about 20,000 cases per year. Thirty six percent of incident ESRD patients received little or no pre-ESRD nephrology care. Mean eGFR at start of dialysis in 2010 was at a peak of 10.4

and went down to 9.8 ml/min/1.73 m2 in 2015. The percentage of incident ESRD cases starting with eGFR at ≥10 ml/min/1.73 m2 rose from 13% in 1996 to 43% in 2010 but decreased afterwards to 39% in 2015 (USRDS, 2017b).

The modality of kidney replacement therapy that was used for incident individuals were as follows: 87.3% began renal replacement therapy with hemodialysis (HD), 9.6% started with peritoneal dialysis (PD), and 2.5% received a kidney transplant (USRDS, 2017b).

Comparisons of Dialysis Methods & Outcomes Needed:

There are two types of dialysis methods for patients, hemodialysis and peritoneal dialysis. Vascular access is essential for hemodialysis patients with ESRD. There are three types of vascular access for hemodialysis patients: the arteriovenous fistula (AVF), arteriovenous graft (AVG) and central venous catheter (CVC) (NIDDK, 2014).

Arteriovenous fistula (AVF) is currently the best type of long-term vascular access in dialysis patients. The surgeon connects an artery to a vein usually in the patient's arm. The artery is the blood vessel that carries blood away from the heart, while the vein is the blood vessel that carries blood back toward the heart. When the surgeon connects an artery to a vein, this helps the vein grow thicker and wider making it easier to place the needles for dialysis. In addition, the AV fistula has a large diameter, this allows faster blood flow in and out of the patient's body providing high blood flow through the dialyzer. AVF is less likely to clot or become infected (NIDDK, 2014).

Arteriovenous graft (AVG) is another form of long-term access for dialysis patients. It is usually formed by a surgeon when encountering problems with the patient's

veins preventing AV fistula creation. It is a man-made tube used to connect the artery with the vein and is associated with higher number of blood clots and infections (NIDDK, 2014).

Central Venous Catheter (CVC) is a small soft tube inserted into a vein in the patient's neck, chest or leg near the groin. It is used in case the kidney disease progresses rapidly or there is no prior placement of vascular access as a temporary method (NIDDK, 2014).

The kidneys do not improve in end stage kidney failure. This results in the patient needing dialysis for the rest of their life. Another option would be kidney transplant, provided that the patient is a candidate for transplant. In hemodialysis, an artificial kidney is used to remove waste, fluids and extra chemicals from the patient's blood. This is done by making an entrance or access into the blood vessels via AVF, AVG or CVC. While in peritoneal dialysis, the blood is cleaned inside the patient's body using a plastic tube (catheter) placed by a physician in the patient's abdomen. During the treatment session, the abdominal area or the peritoneal cavity is slowly filled with dialysate. The blood stays in the arteries and veins in the peritoneal cavity, and all extra fluid and waste products are drawn out of the blood into the dialysate (National Kidney Foundation, 2017a).

In 2015, the most common vascular access used to start dialysis was central venous catheter (CVC) and this represented 80% of patients. There were 68.5% of patients still using catheters at 90 days after hemodialysis initiation. Arteriovenous (AV) fistula use at HD initiation was 17% in 2015 and increased to 65% by the end of the first year on hemodialysis and to 72% by the end of the second year. While AV graft usage for

vascular access was 3% at HD initiation, 15% at one year after initiation, and 16% at two years. The number of patients that were using either an AV fistula or AV graft without the presence of a catheter at one year of hemodialysis initiation was 80% and this number increased to 88% at the end of the second year. Patient age is an important factor contributing to AVF success. Younger age was associated with higher percentage of AV fistulas that successfully matured. Also, the median time to first use of AVF was shorter (USRDS, 2017d).

Systematic Analysis Needed:

The total Medicare fee-for-service spending for the general Medicare population rose by 4.8% to $475.3 billion in 2015. The spending for the end-stage renal disease (ESRD) population increased from $33.1 billion to $33.9 billion, marking a 2.4% rise. This represents 7.1% of the total Medicare paid claims costs, and this number has been the same since 2004. The total inpatient spending showed a rapid increase from 2004 until 2009, this was followed by a slower growth from 2009 until 2011; it has remained the same since then (USRDS, 2017h).

The Dialysis Outcomes and Practice Patterns Study (DOPPS) is a prospective cohort study of hemodialysis practices. The study collects observational and longitudinal data from twenty countries choosing a random sample of patients from a representative and random sample of dialysis facilities. The samples of patients in each facility, and sample of facilities in each country, help provide a valid representation of practices and outcomes in each facility, and in each geographic location (DOPPS, 2018). In the Dialysis Outcomes and Practice Patterns Study (DOPPS), the risk for death was 27.5 per 100 person-year (Bradbury et al., 2007).

End-stage renal disease (ESRD) patients are admitted to the hospital twice a year. Nearly 35% of the patients that are discharged alive may be re-hospitalized during the 30 days following their discharge. Patient hospitalization creates a high financial burden and represents approximately 33% of total Medicare expenditures for dialysis patients. Mortality rates usually increase by age, however, there is inconsistency in hospitalization rates by age. Higher rates were seen in the youngest and oldest age groups (USRDS, 2017e).

Rehospitalization rates for patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD) were at 21.4% and 35.2% respectively. While rehospitalization rates for older Medicare beneficiaries without a kidney disease diagnosis were at 15.4%. In 2015, 37.1% of hospital discharges were followed by a rehospitalization within 30 days among hemodialysis patients (USRDS, 2017e).

The adjusted mortality rates for ESRD, dialysis, and transplant patients were 136, 166, and 29 per 1,000 patient-years in 2015. These mortality rates were 169 for hemodialysis patients and 159 for peritoneal dialysis patients, per 1,000 patient-years when calculated by dialysis modality (USRDS, 2017f).

During the first year of dialysis, mortality patterns were different based on the dialysis modality. Hemodialysis patients had higher mortality rates especially in the second month of treatment, this number decreased afterwards. This was more noticeable in patients that were 65 and older. However, mortality rates for peritoneal dialysis patients was low at the beginning of treatment and increased over time. In addition, the relationship between race and mortality was different considerably when considering the age of the dialysis patients. Moreover, dialysis patients have higher mortality rates when

compared to the general population and Medicare populations with other comorbid diseases such as cancer, diabetes, or cardiovascular disease (USRDS, 2017f).

Identifying factors affecting mortality rate and finding ways to improve outcome can have significant impact on quality of care of ESRD patients and can also reduce hospitalization and healthcare cost during the early period after initiation of dialysis. Timely referral to nephrologist as well as placement of AV fistula are examples of such factors. Improvement in these rates may be related to better dialysis preparation including early placement of dialysis access (Smart & Titus, 2011).

A systematic literature review that discusses outcomes of early versus late nephrology referral in chronic kidney disease is needed. The review highlights the importance of early nephrology referral to reduce mortality and hospitalization which may improve Public Health and practitioner knowledge.

Purpose Statement

The purpose of this thesis is to update and inform general public health and practitioner knowledge regarding interventions that improve dialysis patient outcomes including patient survival and quality of life. Patient morbidity and mortality may be reduced by systematically identifying measures that improve dialysis outcomes. A systematic literature review will help reveal and evolve practices in this area.

Systematic Review:

This thesis will utilize a systematic review with relevant articles and analyze the data available to address the question of how to improve outcome of dialysis patients in the first year which is associated with high mortality, morbidity and healthcare cost. It

will also list recommendations on methods to improve outcome of dialysis patients in the initiation phase.

Systematic review and meta-analysis are considered forms of evidence-based practice. Evidence-based practice (EBP) is the process of integrating the best evidentiary information available with "clinical expertise and client values" (David L. Sackett, Straus, Richardson, Rosenberg, & Haynes, 2000). In 1992 a Canadian medical group first coined the term evidenced-based medicine to describe the usage of best evidence for the care and decision-making process of patients (D. L. Sackett, Rosenberg, Gray, Haynes, & Richardson, 1996). The term evolved to EBP as it caught the attention of those in helping professions such as social work and psychology (Gambrill, 2006). Gibbs describes EBP as (1) being driven by values of putting forth best practices by the researcher or clinician; (2) establishing a well-defined question that guides the research for best practices; (3) exploring and exhausting the literature to answer issues in question; (4) critically appraising the evidence found for validity and worth; (5) applying the evidence to policy or practice; (6) evaluating the effectiveness of the application; and (7) disseminating the results (Gibbs, 2003).

Systematic reviews are used to answer any number of research questions, and subsequent meta-analyses can evaluate data disseminated in multiple quantitative research studies (Littell, Corcoran, & Pillai, 2008). Systematic reviews and meta-analysis often work in tandem but can also be conducted independently. In fact, the appropriateness of conducting a meta-analysis is found through the process of a systematic review. Only quantitative data (e.g., quasi-experimental designs and

randomized control trials) can be used in a meta-analysis while a systematic review of the literature may replicate studies that were conducted qualitatively. In this case, a narrative analysis, also an EBP, would be deemed appropriate for the explication of research findings.

A systematic review involves a specific sequence of repeatable and verifiable steps to examine and produce scientific information. The steps are (1) define the research question; (2) determine the types of studies needed to answer research questions; (3) conduct a comprehensive search of the literature; (4) decide which research can be included or excluded based on inclusionary criteria; (5) critically appraise the included studies; (6) synthesize the studies and assess for homogeneity (discussed in Chapter Three); and (7) disseminate the findings (Petticrew & Roberts, 2006).

Significance Statement

To update and inform general public health and practitioner knowledge by identifying measures that improve mortality, morbidity and lower healthcare cost of incident dialysis patients. This could lead to specific interventions that can make major shifts in thinking and alter the outcome of these patients favorably. Prioritizing attention to specific health issues could help that effort. Increasing AV fistula rate in incident dialysis patients is a key focus of this thesis. Early nephrology referral has also been found to be very important in achieving the above goals.

Chapter 2: Review of literature

Introduction

The purpose of this thesis is to update and inform general public health and practitioner knowledge regarding interventions that improve dialysis patient outcomes including patient survival and quality of life. Patient morbidity and mortality may be reduced by systematically identifying measures that improve public health practitioner knowledge and dialysis outcomes. A systematic literature review may help reveal and evolve practices in this area.

Incident hemodialysis patients have the highest mortality in the first several months after starting dialysis treatments. The most common cause of death in dialysis patients is cardiovascular followed by infectious disease. Understanding the factors that influence such mortality as well as morbidity is key to improving outcome of these incident dialysis patients. Hemodialysis vascular access type has been shown to have great impact on such outcomes.

Body of Review of Literature

Chronic Kidney Disease and end-stage renal disease:

Chronic kidney disease (CKD) is defined as the presence of kidney damage (usually detected as urinary albumin excretion of 30 mg/day or more) or decreased kidney function (defined as an estimated glomerular filtration rate [eGFR] <60 mL/min/1.73 m^2) for three or more months, regardless of the cause. The continuous damage or decreased function for at least three months distinguishes CKD from acute kidney disease. Classification, or staging, of CKD is important in managing these patients

(National Kidney Foundation, 2002). CKD is associated with a higher risk of cardiovascular disease, end-stage renal disease, infection, malignancy, and mortality. ESRD occurs when chronic kidney disease reaches an advanced state. In ESRD the kidneys do not work as they should to meet the body's needs.

Table 1 - Stages of chronic kidney disease (NKF, 2002)

Stage	Description	GFR, mL/min/ 1.73 m2
1	Kidney damage with normal or increased GFR	≥90
2	Kidney damage with mildly decreased GFR	60–89
3	Moderately decreased GFR	30–59
4	Severely decreased GFR	15–29
5	End-stage renal disease	<15 or dialysis

GFR = glomerular filtration rate; mL/min/1.73 m2 = milliliters per minute for 1.73 meters squared

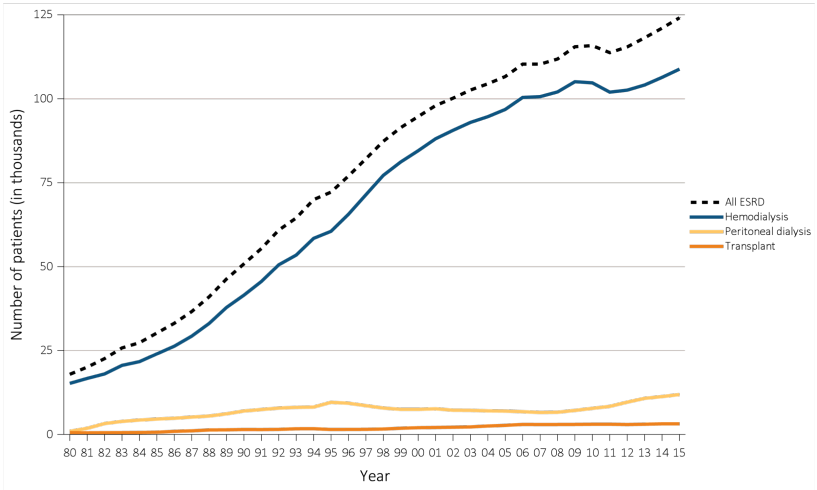
Importance of United States Renal Data System (USRDS):

USRDS has been a valuable data resource to advance knowledge and improve patient care and it will continue to be an important tool for clinicians, investigators, and policy makers. USRDS was first introduced 30 years ago when there was limited ESRD research and it has contributed to a strong scientific basis for epidemiologic and economic research, in addition to applying advanced statistical methodologies related to kidney disease (Port & Held, 2018).

Renal Replacement Options:

ESRD patients can be treated either by dialysis (hemodialysis or peritoneal dialysis) or kidney transplant. In 2015, 87.3% of incident individuals started renal replacement therapy with hemodialysis (HD), 9.6% began with peritoneal dialysis (PD), and 2.5% received a kidney transplant (USRDS, 2017b).

Figure 1 - Trends in the annual number of ESRD incident cases, by modality, in the U.S. population, 1980-2015 (USRDS, 2017)

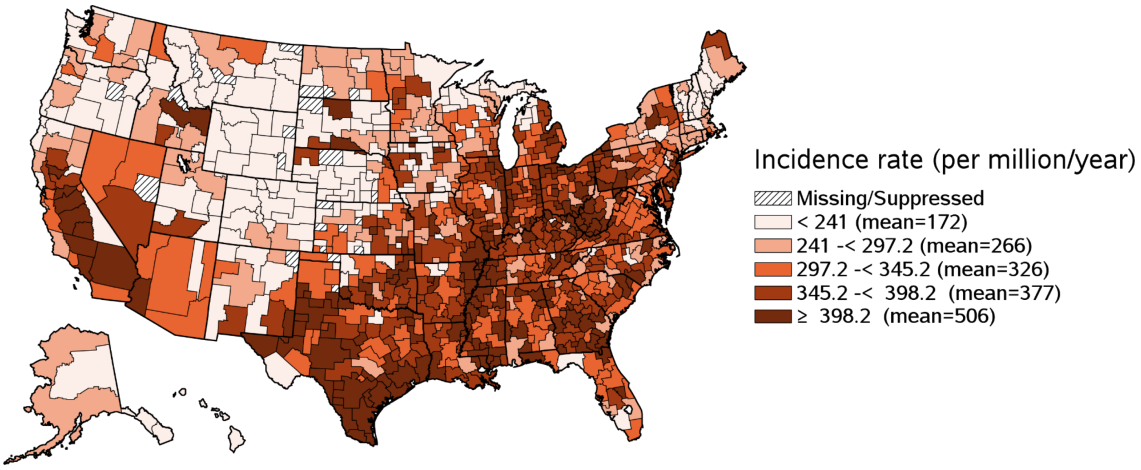


Geographic Distribution in USA:

There is a substantial variation in ESRD incidence rates among the 18 ESRD Networks leading to a major public health issue that includes increased mortality, hospitalization and health care cost. The highest rates were found in parts of the Ohio and Mississippi River valleys, sections of the southeastern U.S., Texas, and California, while

the lowest rates were in areas of New England, the Northwest, and certain Upper Midwest and Rocky Mountain states (USRDS, 2017b).

Figure 2 - Map of the adjusted incidence rate of ESRD, by Health Service Area, in the U.S. population, 2011-2015 (USRDS, 2017)

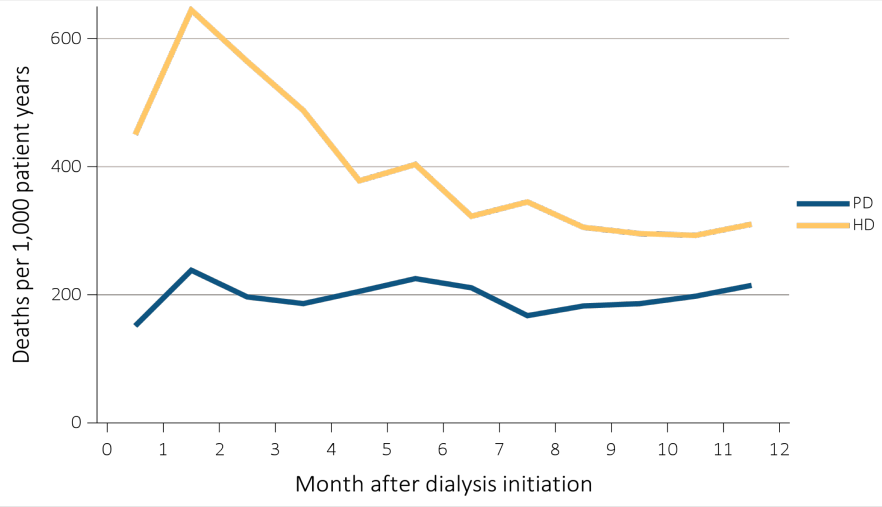


Data Source: Special analyses, USRDS ESRD Database. Standardized for age, sex, and race. The standard population was the U.S. population in 2011. Values for cells with 10 or fewer patients are suppressed. Abbreviation: ESRD, end-stage renal disease.

Mortality:

As compared to the general population and Medicare populations with diabetes, cancer or cardiovascular disease, dialysis patients have significantly higher mortality rates. Mortality patterns during the first year of dialysis were different based on modality. For hemodialysis patients, mortality was highest in month two, but declined afterwards; this effect was more prominent for patients aged 65 and older (USRDS, 2017f).

Figure 3 - Adjusted mortality by treatment modality and number of months after treatment initiation among ESRD patients (a) under age 65 and (b) aged 65 and over, 2014 (USRDS, 2017)

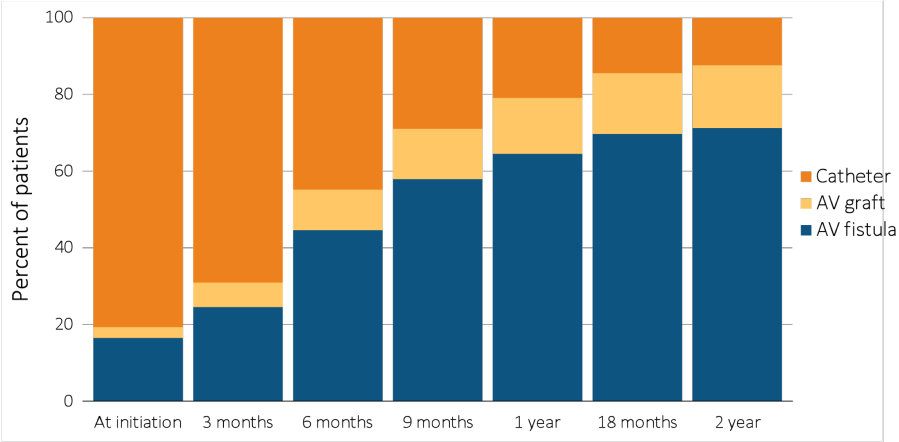


Data Source: Special analyses, USRDS ESRD Database. Adjusted (age, race, sex, ethnicity, and primary diagnosis) mortality among 2013 incident ESRD patients during the first year of therapy. Reference population: incident ESRD patients, 2011. Abbreviations: ESRD, end-stage renal disease; HD, hemodialysis; PD, peritoneal dialysis.

Vascular Access:

Creating permanent vascular access for hemodialysis patients at the start of dialysis is an important treatment challenge. Although established guidelines have all been similar in the recommendation for arterial venous fistula (AVF) as the first choice for treatment, in the Western world, hemodialysis therapy usually starts with a central venous catheter (CVC) (USRDS, 2017d). CVC is usually associated with higher thrombosis and infection rates causing higher mortality, hospitalization and health care cost.

Figure 4 - Change in type of vascular access during the first year of dialysis among patients starting ESRD via hemodialysis in 2013 quarterly: (a) type of vascular access in use (cross-sectional), and (b) longitudinal changes in vascular access use and other outcomes, ESRD Medical Evidence form (CMS 2728) and CROWNWeb, 2013-2016 (USRDS, 2017)

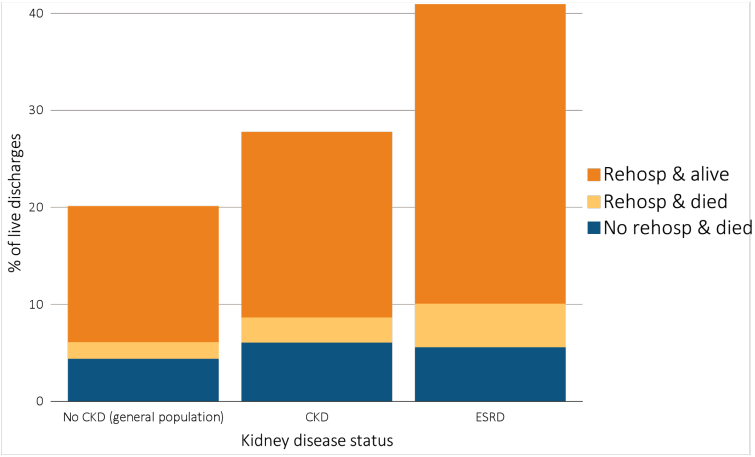


Data Source: Special analyses, USRDS ESRD Database. Data from January 1, 2013 to May 30, 2016: (a) Medical Evidence form (CMS 2728) at initiation and CROWNWeb for subsequent time periods. (b) ESRD patients initiating hemodialysis (N =101,453). Patients with a maturing AV fistula / AV graft with a catheter in place were classified as having a catheter. Abbreviations: AV, arteriovenous; CMS, Centers for Medicare & Medicaid; CROWNWeb, Consolidated Renal Operations in a Web-enabled Network; ESRD, end-stage renal disease; HD, hemodialysis; PD, peritoneal dialysis.

Hospitalization:

The hospitalization rate of CKD and ESRD patients remains unacceptably high as shown by the United States Renal Data System (USRDS). Patients with chronic kidney disease CKD and ESRD experienced rehospitalization rates of 21.4% and 35.2%, as compared to only 15.4% for older Medicare beneficiaries without a kidney disease diagnosis (USRDS, 2017e).

Figure 5 - Proportion of patients aged 66 & older discharged alive from the hospital who were either rehospitalized or died within 30 days of discharge, by kidney disease status, 2015 (USRDS, 2017)

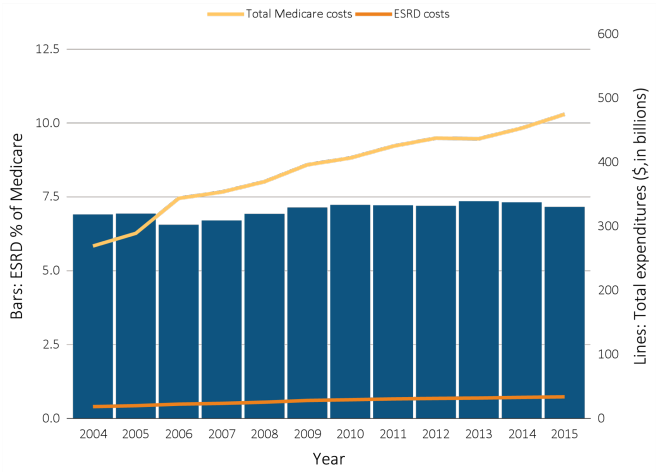


Data Source: Special analyses, USRDS ESRD Database and Medicare 5% sample. January 1, 2015 point prevalent Medicare patients aged 66 & older on December 31, 2013. For general Medicare: January 1, 2015 point prevalent, Medicare patients aged 66 & older, discharged alive from an all-cause index hospitalization between January 1, 2015, and December 1, 2014, unadjusted. CKD determined using claims for 2014. Abbreviations: CKD, chronic kidney disease; ESRD, end-stage renal disease; rehosp, rehospitalization.

Health care cost:

The Medicare program for the elderly started in 1965 and by 1972, Medicare eligibility included both disabled persons aged 18 to 64 and individuals with irreversible kidney disease who required dialysis or transplant. At that time, there were only about 10,000 individuals treated with dialysis. This patient group grew to 434,914 in 2015. The Medicare fee-for-service spending for the ESRD population accounts for 7% of the overall Medicare paid claims costs even though they represent only 1% of the total Medicare population (USRDS, 2017h).

Figure 6 - Trends in costs of the Medicare & ESRD programs, 2004-2015 (USRDS, 2017)



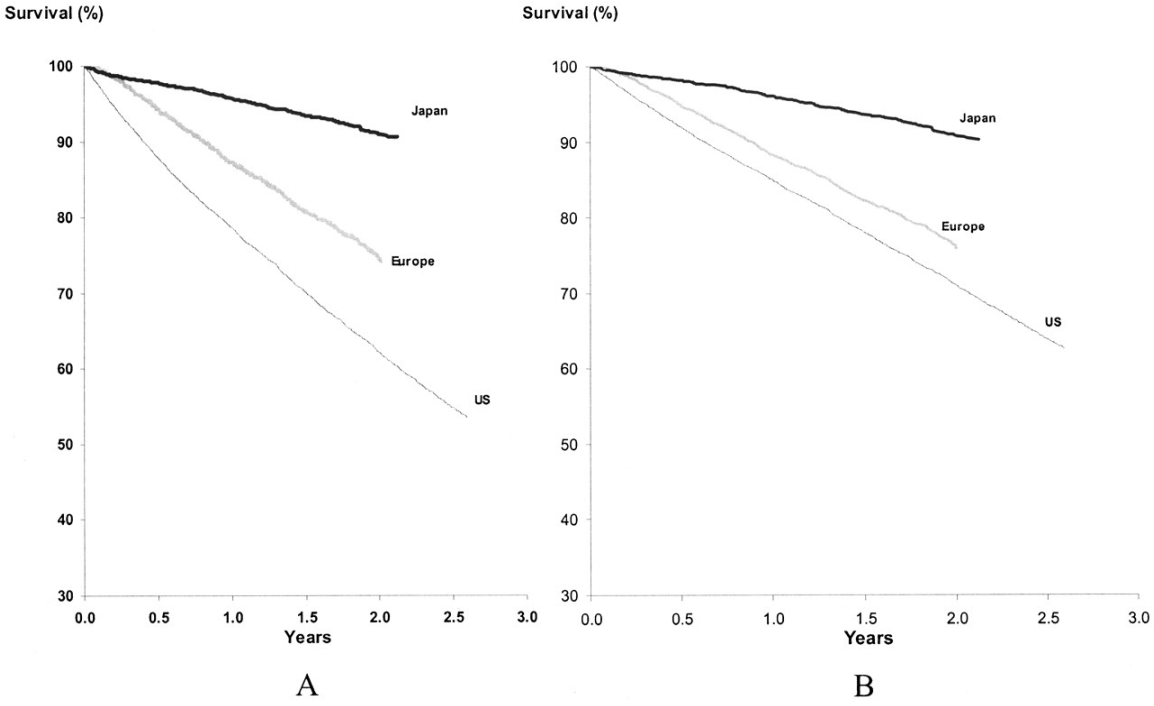
Data Source: Total ESRD costs obtained from USRDS ESRD Database; Reference Table K.1. Total Medicare expenditures obtained from Trustees Report, Table II.B1 https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/ReportsTrustFunds/TrusteesReports.html. Abbreviation: ESRD, end-stage renal disease.

International Comparison:

In the Dialysis Outcome and Practice Pattern Study (DOPPS), the crude 1-yr mortality rates of hemodialysis patients were 6.6% in Japan, 15.6% in Europe, and 21.7% in the US. According to the study, the relative risk (RR) of mortality was 2.84 ($P < 0.0001$) for Europe compared with Japan (reference group) and was 3.78 ($P < 0.0001$) for the US compared with Japan after adjusting for age, gender, race, and 25 comorbid conditions. While the adjusted RR of mortality for the US versus Europe was 1.33 ($P < 0.0001$) (Goodkin et al., 2003).

There is wide variability in AV fistula rate among different countries. A 2002 report from DOPPS highlighted that 83% of German dialysis patients initiated dialysis with a fistula, compared with 69% in Spain and only 15% in the United States (Foley & Hakim, 2009).

Figure 7 – Cox survival curves by continent: (A) unadjusted and (B) adjusted for patient demographics and comorbidities listed in Table 3. (Goodkin et al., 2003)



Summary of Current Problem and Study Relevance

Despite the progress that was made in improving AVF rate as well as mortality outcome in the US, these outcome measures remain markedly unfavorable compared to the same outcome measures in Japan and Europe as demonstrated by DOPPS study. Identifying factors that affect such outcomes is crucial to improving these outcomes in the US.

This study examines the factors that lead to improved AVF rate and mortality rate. Leveraging information technology to improve early nephrology referral and patient education is an example of such factors or interventions.

Early referral of patients to nephrologists is optimal, although nephrologists cannot exclusively manage all patients with CKD. The burden of CKD management thus falls largely on Primary Care Physicians due to their limited awareness of CKD. Future focus should be on increasing CKD awareness and management among mid-level providers in addition to awareness of the KDOQI guidelines among these health care practitioners. Educational efforts improving CKD awareness in training programs might be beneficial as well (Plantinga, Tuot, & Powe, 2010).

Public policy has a major role in affecting patient and provider awareness. World Kidney Day is an annual event sponsored by both the National Kidney Foundation (NKF) and International Society of Nephrology and was launched in 2006. Its aim is "to raise awareness of the importance of our kidneys to our overall health and to reduce the frequency and impact of kidney disease and its associated health problems worldwide." This can be done by raising awareness in the community through providing free screening and education about CKD, its risk factors, and consequences (Plantinga et al., 2010).

In addition, the NKF has launched a free screening program called, The Kidney Early Evaluation Program (KEEP). It focuses on individuals that are at high risk for developing CKD. These risk factors include, individual's age of 18 years or older, hypertension, diabetes, and/or family history of CKD. KEEP has screened more than 130,000 individuals throughout the United States since its establishment in 1997. Both of

these NKF efforts have helped increase general knowledge of CKD and improved awareness of disease status among patients (Plantinga et al., 2010).

Chapter 3: Methodology

Introduction

The purpose of this thesis is to update and inform general public health and practitioner knowledge regarding interventions that improve dialysis patient outcomes including patient survival and quality of life. Patient morbidity and mortality may be reduced by systematically identifying measures that improve dialysis outcomes. A systematic literature review will help reveal and evolve practices in this area.

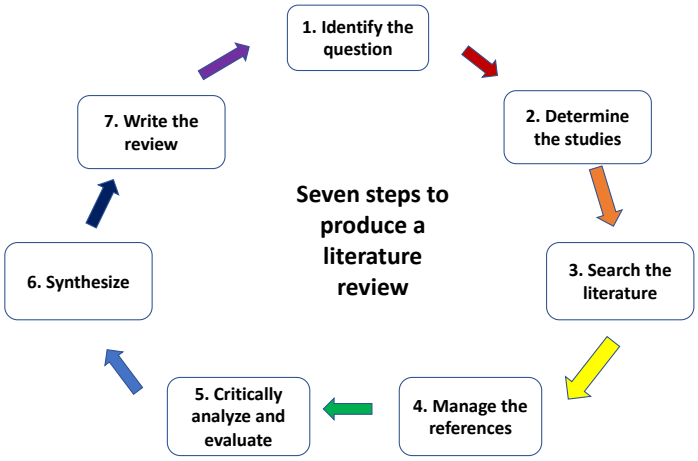
This chapter includes a complete description and step by step process of the systematic literature review conducted. This chapter includes the specific search terms, exclusion and inclusion criteria and the creation of PRISMA chart to obtain the final list of articles studied. PRISMA stands for Preferred Reporting Items for Systematic Reviews and Meta-Analyses. It is a tool used for outlining evidence-based items in systematic reviews and meta-analyses. The aim of the PRISMA Statement is to help authors standardize and improve the reporting of systematic reviews and meta-analyses.

A systematic review was conducted as a means to thoroughly examine the research and literature to date with a focus on peer reviewed literature over the past 15 years. A systematic review is particularly pertinent to research in which there is uncertainty about the outcome of the effectiveness of an intervention.

Petticrew and Roberts discuss seven steps for a systematic review. These steps are: (1) clearly define the research question or hypothesis; (2) determine the types of studies needed to carry out the study; (3) perform a comprehensive literature search needed to locate the studies; (4) screen the studies located and assess if they meet the

inclusionary criteria or if they require further analysis; (5) critically appraise the studies that will be included in the systematic review; (6) synthesize the studies and assess for homogeneity; and (7) disseminate the outcome of the review (Petticrew & Roberts, 2006). The process is demonstrated in Figure 8 below.

Figure 8 – Steps to Produce a Literature Review



Literature Search Methodology

In order to examine the topic, PubMed was selected because this database contains a wide variety of public health research journal articles. The keyword search terms in PubMed developed for this systematic literature review were:
early AND (dialysis OR hemodialysis) AND (end stage renal disease OR ESRD OR chronic kidney failure) AND Arteriovenous fistul* AND mortality.

Eligibility Criteria:

Fifty-two (52) articles were found searching the database with the appropriate search string, the articles were imported within EndNote™. After reading the article titles and literature abstracts, these articles were narrowed down using the following inclusion and exclusion terms based on the research questions.

Inclusion/Exclusion Criteria:

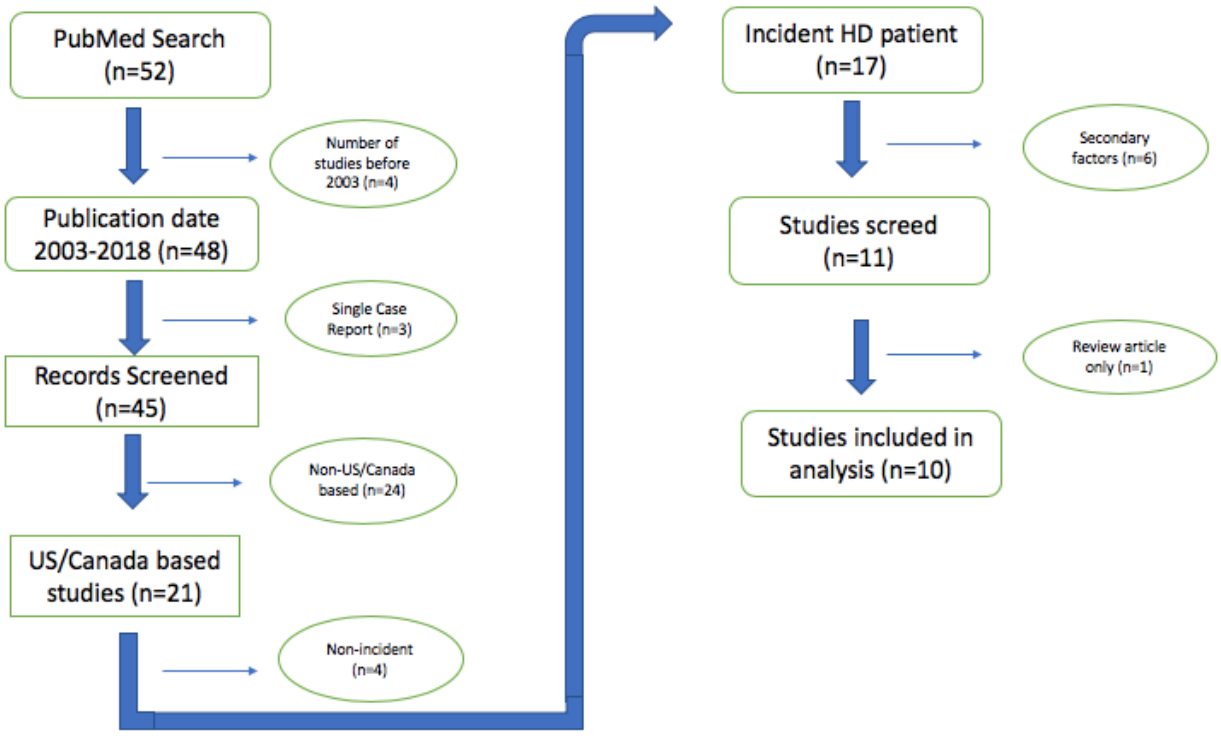
For this systematic literature review, a PubMed Search was done to find studies that examined data regarding the topic being analyzed. This resulted in 52 articles for review. After initial screening, four articles were excluded as these were published before 2003. It was decided to examine studies that were published over the past 15 years (between 2003-2018). Three other articles were excluded as these were single case reports providing limited information for the overall analysis.

Due to marked differences in AV fistula rate and outcome measures between US/Canada and non-US/Canada based studies, the studies to be examined were limited to US/Canada-based studies to make the findings of this systematic review more relevant and accurate for this hemodialysis patient population. There were as many as 24 studies that were not based in the United States and Canada. This resulted in a total of 21 articles based in North America. After full text screening, four articles that studied non-incident hemodialysis patients were excluded. Including non-incident hemodialysis patients would have confounded the results given the narrow focus of this systematic review on patients starting hemodialysis. This resulted in 17 articles. In addition, and after full text review, six articles that looked at factors that either were not relevant to the question addressed by the systemic review or were unlikely to affect significantly the main outcome

measures were excluded. For example, one study examined how surgical technique affects AV fistula creation before dialysis initiation and did not address outcome after patients-initiated dialysis.

Finally, one article was a review article and did not include original or new data and therefore, it was excluded. This resulted in a total of ten articles for review on the proposed topic.

Figure 9 – PRISMA Chart



Data Extraction and quality assurance

The next step in this systematic literature review was reading the full text of the ten articles chosen and extracting relevant data. The variables studied for this analysis included, study number, title, authors, study type, early nephrology referral, mortality hazard ratio (HR) AVF, mortality HR AVG and mortality HR CVC. Afterwards, the data were entered directly into an excel sheet with the different variables to help with the analyzation process (Table 2).

Study No.	Title	Authors	Study Type	early nephrology referral	Mortality HR AVF	Mortality HR AVG	Mortality HR CVC
1	Dispartities in early mortality among chronic kidney disease patients who transition to peritoneal dialysis and hemodialysis with and without catheters	Sim et al.	Retrospective Cohort	More aggressive and timely management strategies such as earlier and more frequent nephrology	1.87	1.87	2.77
2	Dialysis Access as an area of improvement in Elderly Incident Hemodialysis patients (DOPPS)	Raimann et al.	Cohort study from the International Monitoring Dialysis Outcomes Initiative	Early preperation for dialysis initiation must become a focus of clinical nephrology	1.92 (CVC --> AVG/AVF 6 months)	1.92 (CVC --> AVG/AVF 6 months)	2.89 (CVC -->CVC 6months)
3	Pre-End stage renal disease care and early survival among incident dialysi spatients in the US Military Health System	Nee, Fisher, Yuan, Agodoa, & Abbott	Retrospective Cohort	early nephrology referral may be a contributor to better outcome in MHS population	See text	See text	See text
4	Vascular Access Type, Inflammatory Markers, and Mortality in Incident Hemoldialysis Patients (CHOICE) Study	Banerjee et al.	cohort study post hoc analysis of CHOICE study	Not mentioned	1.00	1.40	1.76
5	PD is not a superior therpay to HD/ Hemodialysis Vascular Access Modifies the association betweendialysis modality and survival	Stokes, J / Perl et al.	Review article/ registry based observational cohort study	Differences between patients well prepared for dialysis versus not well prepared	1.00	1.00	1.80
6	Coversion of vascular access type among incident HD pts	Bradbury, B et al.	Retrospective Cohort study	Continued efforts to increase early nephrology referral and permenant vascular access placement may help decrease mortality	0.64 CVC to AVF	0.71 CVC to AVG	1.81 AVF to CVC 1.55 AVG to CVC
7	Catheter related mortality among ESRD patients	Wasse et al. / Xue et al.	Retrospective study	Not mentioned	1.00	1.09	1.70
8	AVF use association with lower CV mortaility compared with catheter use among ESRD patients	Wasse et al.	Retrospective study	Not mentioned	0.57	0.87	1.00
9	Association of clinic vascular accesss monitoring practices with clinical outcomes in HD pts	Plantinga et al.	Prospective cohort study	Monitoring vascular access on a regular basis requires more frequent interaction with nephrology care team	see text	see text	see text
10	Type of vascular access and survival among incident HD pts (CHOICE)	Astor et al.	Observational study	Patients using an AVG or CVC were more likely to have been referred late to a nephrologist as compared to patients using AVF	1.00	1.21	1.47

Table 2 – Summary of articles for systematic review

Analysis Review

After ensuring that all relevant articles were captured through the systematic literature search, each article was analyzed in the spreadsheet created. The data analysis included variables that were common to the studies and variables that were missing from the studies.

Variables that were common to the studies were mortality among incident hemodialysis patients who started with AVF vs. AVG vs. CVC. One additional variable that was common to the studies, was timely referral to nephrologist before initiation of dialysis. This was associated with higher predialysis AVF placement which reduced mortality.

Variables that were consistently missing from the studies included, hospitalization, inflammation or infection leading to hospitalization and health care cost.

Based upon this analysis, it appears that the variables that will be most useful for results comparisons will be mortality in the first 6-12 months with CVC, mortality in the first 6-12 months with AVG and mortality in the first 6-12 months with AVF.

It was noted that some studies lacked uniformity regarding their methodology. Notations were made regarding variables and factors that may have been included or excluded from the study. As discussed further in the next chapter, this may have implications for general public health and practitioner knowledge as well as public health practices.

Chapter 4: Results

Introduction

The purpose of this thesis was to update and inform general public health and practitioner knowledge regarding interventions that improve dialysis patient outcomes including patient survival and quality of life. Patient morbidity and mortality may be reduced by systematically identifying measures that improve dialysis outcomes. A systematic literature review will help reveal and evolve practices in this area.

A PubMed search was conducted using the search criteria provided in Chapter 3. Fifty-two (52) articles were identified for potential inclusion in the study. Articles were then screened and included/excluded based on the PRISMA criteria outlined by the methodology. These criteria included: publication date, single case reports, review articles only, studies that were not based in the US/Canada, non-incident hemodialysis patients and secondary factors not related to the topic addressed. For additional review of the methodology, please refer to the PRISMA chart included in Chapter 3. Based upon the PRISMA criteria, ten articles were analyzed for detailed review.

Study Characteristics

All ten articles identified by the systematic literature review were peer-review articles that used quantitative methods to analyze the data and discuss the findings to prove the hypothesis of the study conducted. They were retrospective cohort studies that included large random samples that were studied within a given timeframe. The studies were based in US/Canada.

Tables/figures that support analysis

Table 2. provides a summary to aid a better understanding to the outcomes/results of the systematic literature review analysis findings. The table highlights the different variables that looked at mortality in the first 6-12 months with CVC, mortality in the first 6-12 months with AVG and mortality in the first 6-12 months with AVF. It also, demonstrates the consistent need for early nephrology care and optimal vascular access method to improve patient mortality and outcome.

Study No.	Title	Authors	Study Type	early nephrology referral	Mortality HR AVF	Mortality HR AVG	Mortality HR CVC
1	Dispartities in early mortality among chronic kidney disease patients who transition to peritoneal dialysis and hemodialysis with and without catheters	Sim et al.	Retrospective Cohort	More aggressive and timely management strategies such as earlier and more frequent nephrology	1.87	1.87	2.77
2	Dialysis Access as an area of improvement in Elderly Incident Hemodialysis patients (DOPPS)	Raimann et al.	Cohort study from the International Monitoring Dialysis Outcomes Initiative	Early preperation for dialysis initiation must become a focus of clinical nephrology	1.92 (CVC --> AVG/AVF 6 months)	1.92 (CVC --> AVG/AVF 6 months)	2.89 (CVC -->CVC 6months)
3	Pre-End stage renal disease care and early survival among incident dialysi spatients in the US Military Health System	Nee, Fisher, Yuan, Agodoa, & Abbott	Retrospective Cohort	early nephrology referral may be a contributor to better outcome in MHS population	See text	See text	See text
4	Vascular Access Type, Inflammatory Markers, and Mortality in Incident Hemoldialysis Patients (CHOICE) Study	Banerjee et al.	cohort study post hoc analysis of CHOICE study	Not mentioned	1.00	1.40	1.76
5	PD is not a superior therpay to HD/ Hemodialysis Vascular Access Modifies the association betweendialysis modality and survival	Stokes, J / Perl et al.	Review article/ registry based observational cohort study	Differences between patients well prepared for dialysis versus not well prepared	1.00	1.00	1.80
6	Coversion of vascular access type among incident HD pts	Bradbury, B et al.	Retrospective Cohort study	Continued efforts to increase early nephrology referral and permenant vascular access placement may help decrease mortality	0.64 CVC to AVF	0.71 CVC to AVG	1.81 AVF to CVC 1.55 AVG to CVC
7	Catheter related mortality among ESRD patients	Wasse et al. / Xue et al.	Retrospective study	Not mentioned	1.00	1.09	1.70
8	AVF use association with lower CV mortaility compared with catheter use among ESRD patients	Wasse et al.	Retrospective study	Not mentioned	0.57	0.87	1.00
9	Association of clinic vascular accesss monitoring practices with clinical outcomes in HD pts	Plantinga et al.	Prospective cohort study	Monitoring vascular access on a regular basis requires more frequent interaction with nephrology care team	see text	see text	see text
10	Type of vascular access and survival among incident HD pts (CHOICE)	Astor et al.	Observational study	Patients using an AVG or CVC were more likely to have been referred late to a nephrologist as compared to patients using AVF	1.00	1.21	1.47

Table 2 – Summary of articles for systematic review

Analysis of major themes and findings

The variables that were examined and used for comparison were, mortality in the first 6-12 months with CVC, mortality in the first 6-12 months with AVG and mortality in the first 6-12 months with AVF. Additionally, when studies lacked uniformity regarding their methodology notations were made regarding variables and factors that may have been included or excluded from the study. Analysis of results produced findings in several categories. These categories are noted and discussed below.

Variables that were common to the studies:

The common outcome variables in all studies were mortality among incident hemodialysis patients who started with AVF vs. AVG vs. CVC and timely referral to nephrologist.

When calculating hazard ratio (HR) of mortality, the majority of the studies used the HR mortality for AVF as the reference. One study titled, Arteriovenous fistula use is associated with lower cardiovascular mortality compared with catheter use among ESRD patient, used the HR CVC as the reference (Wasse, Speckman, & McClellan, 2008).

Mortality based on vascular access type:

The ten studies highlighted this variable in the results and calculated the hazard ratio to come to the conclusion of the importance of vascular access type.

Peritoneal Dialysis Is Not a Superior Therapy to Hemodialysis: A Comparison (Stokes, 2012), is a review article. The article did not include any specific data regarding outcome but reflects the author's observations and comparison between hemodialysis and peritoneal dialysis. The author referenced another article that hemodialysis vascular access modifies the association between dialysis modality and survival (Perl et al., 2011).

The study acknowledged that when compared with 7412 PD patients, the 1-year mortality rate for 6663 HD-AVF/AVG patients was similar to the peritoneal dialysis patients but was 80% higher for the 24,437 HD-CVC patients (adjusted HR, 1.8; 95% confidence intervals [CI], 1.6 to 1.9). It also demonstrated that when measured to peritoneal dialysis patients, hemodialysis patients with AVF/AVG had a lower risk of death than patients with CVC. In conclusion, the use of CVC in incident HD patients had a major role in the early survival rates seen with PD patients (Perl et al., 2011).

Disparities in early mortality among chronic kidney disease patients who transition to peritoneal dialysis and hemodialysis with and without catheters (Sim et al., 2018), the authors found that the adjusted 6-month mortality HRs (95% CI) were 1.87 (1.06–3.30) and 3.77 (2.17–6.57) for HD with AVF/AVG and HD with a catheter, respectively. These results indicate that among the CKD population who transitioned to ESRD, there was a high mortality rate immediately after the start of dialysis especially among hemodialysis patients who transitioned with a catheter (Sim et al., 2018).

Dialysis Access as an Area of Improvement in Elderly Incident Hemodialysis Patients: Results from a Cohort Study from the International Monitoring Dialysis Outcomes Initiative (DOPPS) (Raimann et al., 2017), showed the highest risk of death was among those starting dialysis with a CVC without conversion to a non- CVC access in patients between the age of 70 and 80 in addition to patients that are 80 years and older. This was particularly noticed in patients older than 79 years. Dialysis initiation with AVF/AVG and at 6 months AVF/AVG was used as reference. The results showed a Hazard Ratio (HR) of 2.89 for dialysis initiation with CVC and CVC at 6 months, HR of

1.92 for dialysis initiation with CVC and AVF/AVG at 6 months and HR of 0.96 for dialysis initiation with AVF/AVG and CVC at month 6 (Raimann et al., 2017).

Pre-End-Stage Renal Disease Care and Early Survival among Incident Dialysis Patients in the US Military Health System (MHS) (Nee, Fisher, Yuan, Agodoa, & Abbott, 2017), studied the mortality risk at 6 months compared to baseline (non- MHS). The adjusted hazard ratio AHR was 0.64. However, after adjusting for pre-ESRD nephrology care and vascular access type, the AHR was only 0.79 which was not statistically significant. This might indicate that these two parameters are very important and account for most if not all the AHR survival advantage of MHS patients over non- MHS (Nee et al., 2017).

Conversion of Vascular Access Type Among Incident Hemodialysis Patients: Description and Association with Mortality (Bradbury et al., 2009), suggested that there was accumulating evidence that the type of vascular access at HD initiation is strongly related to future infectious complications, central venous stenosis and mortality risk. HR mortality when conversion occurs from CVC to AVF is 0.64 and 0.71 when conversion occurs from CVC to AVG. While HR mortality when conversion from AVF to CVC is 1.81 and when conversion from AVG to CVC is 1.55 (Bradbury et al., 2009).

Association of Clinic Vascular Access Monitoring Practices with Clinical Outcomes in Hemodialysis Patients (Plantinga et al., 2006), concluded that frequent monitoring of dialysis access may initially increase the number of interventions but is beneficial to longer-term outcomes, including septicemia related and all-cause hospitalization. In the overall population of patients with grafts and fistulas, there was no statistically significant association of routine or more frequent monitoring with all-cause

mortality. This may be expected since the mechanism through which access monitoring might affect certain causes of mortality (e.g., cardiovascular causes or cancer) is unclear. (Plantinga et al., 2006).

Type of vascular access and survival among incident HD patients (CHOICE) study demonstrated that incident hemodialysis patients who were using a venous catheter were at a 47% higher risk for death compared to their counterparts who were using AVF (Astor et al., 2005). The adjusted hazard ratio (HR) was 1.0 (reference) for AVF, 1.21 for AVG and 1.47 for CVC. These results strongly support existing clinical practice guidelines and suggest that the use of venous catheters should be minimized to improve patient survival and reduce the frequency of access complications (Astor et al., 2005).

Vascular Access Type, Inflammatory Markers, and Mortality in Incident Hemodialysis Patients: The Choices for Healthy Outcomes in Caring for End-Stage Renal Disease (CHOICE) Study (Banerjee et al., 2014), studied the relationship between inflammatory markers, access type and mortality. The difference between the different types of vascular accesses gets smaller after correcting for inflammatory markers of C-reactive protein and Interleukin six. This suggests that the cause of increased mortality is increased inflammatory state in CVC and to lesser extent AVG compared to AVF. The unadjusted relative hazard of mortality by AVF was 1.00 (reference), 1.40 for AVG and 1.76 for CVC (Banerjee et al., 2014).

Catheter Related Mortality in ESRD patients (Wasse, 2008), the author referenced a study, The Association of Initial Hemodialysis Access Type with Mortality Outcomes in elderly Medicare ESRD patients (Xue, Dahl, Ebben, & Collins, 2003). This study concluded that in the US Medicare dialysis population, type of hemodialysis access is

associated with mortality risk. The HR mortality for AVF was 1.00, 1.09 in AVG and 1.70 in CVC (Xue et al., 2003).

Arteriovenous use association with lower cardiovascular mortality compared with catheter use among ESRD patients (Wasse et al., 2008), the study concluded the strong correlation between arteriovenous fistula use and decreased all-cause and cardiovascular mortality. After considering several variables, cardiovascular mortality was significantly lower in AVF use 90 days after starting dialysis as compared to catheter use. These findings indicate that vascular access type has a significant role in cause-specific mortality beyond that of infection and supports the recommendation of AVF use in the early phases of chronic end-stage renal disease therapy per existing guidelines. The hazard ratio (HR) for cardiovascular related mortality using CVC was at 1.00 (reference), HR mortality with AVG was at 0.87 and HR mortality with AVF was at 0.57 (Wasse et al., 2008).

Early Nephrology Referral Needed:

Timely referral to nephrologist before initiation of dialysis could play a significant role in facilitating proper pre-ESRD care which would be conducive to more AVF placement and therefore lower mortality. This relationship was outlined in seven out of the ten studies but was missing from three studies. The sooner that CKD patients are referred to a nephrologist, the more likely they will initiate dialysis with AVF and therefore have lower mortality.

Variables that were missing from the studies:

Some studies included additional outcome variables that were missing in the other studies. These variables include, hospitalization, inflammation or infection leading to hospitalization and health care cost.

Hospitalization for different reasons such as vascular access thrombosis or infections is an important outcome measure. Plantinga et al., observed that routine monitoring of vascular access was associated with decreased all-cause hospitalization in patients with fistulas but not in patients with AV grafts. There was a 65% decrease in hospital admission for septicemia with regular vascular access monitoring relative to no monitoring. This association was more pronounced in patients with AVF vs. patients with AVGs.

Infection rate in patients with different vascular access is another important outcome variable. Wasse et al., outlined infection rates due to different types of infections including bacteremia, endocarditis, septic shock, septic arthritis and epidural abscess.

Inflammatory markers such as CRP and IL-6 can be quite predictive of outcome. Banerjee et al., outlined that these inflammatory markers were found to account for most of the mortality difference between patients initiating HD with CVC vs. AVF. This suggests that inflammation might be the underlying cause of the difference in mortality between these two patient populations.

Healthcare cost was not addressed in these studies even though this variable has great impact on public health decisions given the high cost of such therapy. USRDS outlines healthcare cost per Medicare dialysis patient's PD vs. HD. Conducting studies

that review impact of healthcare cost on these patients can help tremendously in highlighting the importance of early AVF placement to improve patient outcome.

Results Summary

The systematic review produced the following conclusions:

- Early referral to nephrologist is very important to improve patient outcomes, it provides better dialysis preparation and early placement of AV fistula. Providing structured programs for prompt educational and medical strategies in early end-stage renal disease patients is promising and has potential benefits.
- Improving vascular access for incident hemodialysis patients is an important fundamental consideration. This can be accomplished by increasing the percentage of adult hemodialysis patients who use arteriovenous fistulas as the primary mode of vascular access at the start of hemodialysis and reducing the percentage of adult hemodialysis patients who use central venous catheters at the start of renal replacement therapy which is associated with higher infection rate, thrombosis and mortality.
- Disparities exist between different types of patients. These disparities may be able to be actionably addressed through improved public health and provider education.

The implications of these results are discussed further in the next chapter.

Chapter 5: Discussion

Introduction

The purpose of this thesis was to update and inform general public health and practitioner knowledge regarding interventions that improve dialysis patient outcomes including patient survival and quality of life. Patient morbidity and mortality may be reduced by systematically identifying measures that improve dialysis outcomes. A systematic literature review will help reveal and evolve practices in this area.

Summary of key study findings

This study highlighted important measures to improve outcome for patients starting dialysis. Delay in AVF placement lead to increased dependence on catheter access which contributed significantly to increased morbidity, mortality and cost of providing hemodialysis. The timing of AVF placement and avoidance of catheter access was critical to the successful transition from chronic kidney disease (CKD) to ESRD with hemodialysis (Hammes, 2017).

Limitations

It is noted that there are a number of considerations that are outlined below which may limit the ability to generalize these findings.

First, this thesis included studies based in North America and its results might not be relevant to other countries or patient populations. Second, it focused on incident hemodialysis patients and consequently it might not be applicable to prevalent hemodialysis patients. Third, previous studies showed that AV fistula creation and maturation is less successful in certain patient subgroups such as diabetic patients and

those with severe vascular disease (Goodkin et al., 2003). These subgroups have poor outcome due to cardiovascular disease. Therefore, a selection bias might explain the difference in outcome in these patient subgroups rather than AVF status.

Some studies in this systematic literature review included additional outcome variables that were missing in other studies. These variables included, hospitalization, inflammation or infection leading to hospitalization and increased health care cost. This data would have been extremely beneficial in better understanding of the problem addressed and providing stronger evidence for the need of early interventions to improve patient outcome.

Implications

Implications for General Public Health and Practitioner Practice:

Improving general public health and practitioner knowledge regarding interventions that improve dialysis patient outcomes will have great impact on patient survival. Patient morbidity and mortality may decrease significantly which leads to improving their quality of life. This will also have a great effect on reducing health care cost associated with late AVF dialysis initiation.

Implications for public health practice:

The implications for public health practice are to improve vascular access of incident hemodialysis patients. This can be done by increasing the percentage of adult hemodialysis patients who use arteriovenous fistulas as the primary mode of vascular access at the start of hemodialysis and reducing the percentage of adult hemodialysis patients who use central venous catheters at the start of renal replacement therapy which is associated with higher infection rate, thrombosis and mortality.

Early referral to nephrologist is also very important to improve outcome by providing better dialysis preparation and early placement of AV fistula. Providing structured programs for prompt educational and medical strategies in early end stage renal disease patients is promising and has potential benefits.

Recommendations

General Public Health Education:

To improve vascular access of incident hemodialysis patients, public health can help increase the percentage of adult hemodialysis patients who use arteriovenous fistulas as the primary mode of vascular access at the start of hemodialysis. This can be achieved by better promoting awareness through events such as World Kidney Day (World Kidney Day, 2019).

To increase early referral to nephrologist, public health can provide education and structured programs for chronic kidney disease patients. An example of such programs is the Kidney Early Evaluation program (KEEP).

Clinician Education:

Most patients with early stage CKD can be managed by their primary care physician (PCP). Routine follow up visits with the PCP help identify patients that are at high risk of developing chronic kidney disease that may progress to end stage renal disease. Primary care providers must continue to work together with nephrologists to improve the lives of those living with CKD. Due to the importance of this public health issue, early detection and prevention of CKD through primary care is very important. Primary care providers (PCPs) are well positioned to manage most CKD cases independently given that most patients are at low risk of progression to ESRD. Timely

referral to nephrologist for patients with CKD who do progress to advanced stages is associated with better patient outcomes and experiences along their care journey. Helping PCPs determine which patients are at high risk of developing CKD to properly diagnose and manage the disease in order to reduce the risk of further progression is essential. Creating a tool kit such as the KidneyWise clinical toolkit created by The Ontario Renal Network can be helpful. It provides an evidence-based clinical algorithm which offers a step-by-step approach to the identification and management of CKD. This toolkit can help determine when referral to a nephrologist is appropriate (Grill & Brimble, 2018).

Patient Education:

Lack of patient education regarding disease status results in patients not equipped to make important decisions related to CKD and ESRD. These decisions include early AVF placement. Delays in care due to poor knowledge, leave patients susceptible to complications of the disease. For patients to make informed choices of dialysis modality, they need to understand kidney disease itself. This can help increase patient compliance and improve patient outcome (Fishbane, Hazzan, Halinski, & Mathew, 2015).

Enhancements to informatics (Electronic Health Records):

The office of the US President, National Institutes of Health, Food and Drug Administration, Office of the National Coordinator for Health Information Technology, and other stakeholders introduced the Precision Medicine Initiative in 2016 as a comprehensive approach that studies individuals' uniqueness and differences in their biology, genetics, lifestyle, and environment to prevent and treat disease. The ultimate goal is to personalize and identify methods of treatment that are distinctive to each individual (Rhee, Obi, Mathew, & Kalantar-Zadeh, 2018).

Precision medicine has been a common interest in nephrology and especially in the care of patients with advanced chronic kidney disease and end stage kidney disease. Using a comprehensive personalized approach examining the patient's medical history, lifestyle factors (e.g., diet, physical activity, health behaviors), environment (e.g., geographic location, social support), and personal factors is important to choose the best treatment plan (e.g., hemodialysis versus peritoneal dialysis, kidney transplantation, conservative management) for each individual (Figure 10) (Rhee et al., 2018).

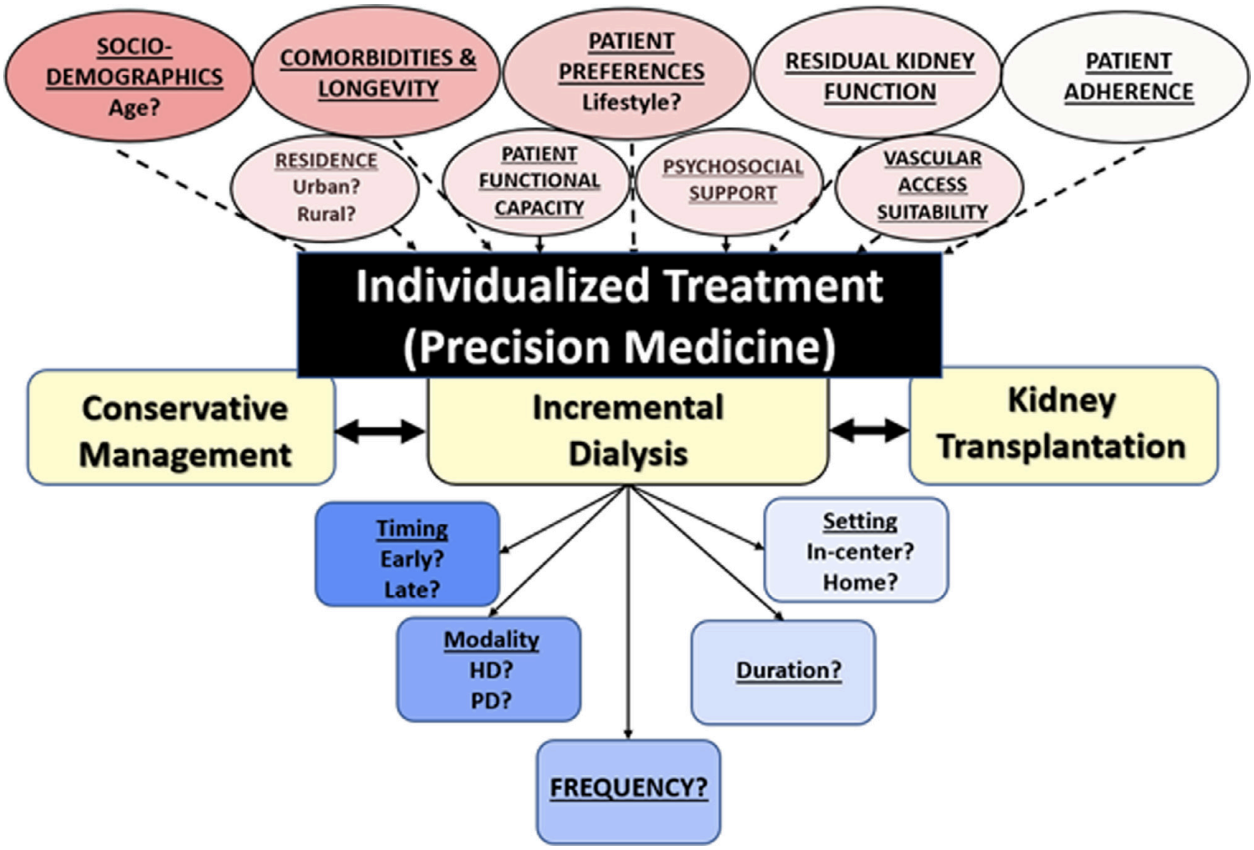


Figure 10 - Personalized approach in the transition to renal replacement therapy

Creating a health information exchange system that would allow data from dialysis organizations, vascular access centers and healthcare providers organizations to

be centralized will facilitate improved patient monitoring and management. It will help consider all clinical, demographic, biologic and process of care predictors for arteriovenous fistula maturation and improve patient outcome. This will result in a patient-centric, precision medicine approach to vascular access dysfunction. Tailoring treatment based on the individual will have an important effect on both clinical practice and patient quality of life (Figure 11) (Roy-Chaudhury, 2016).

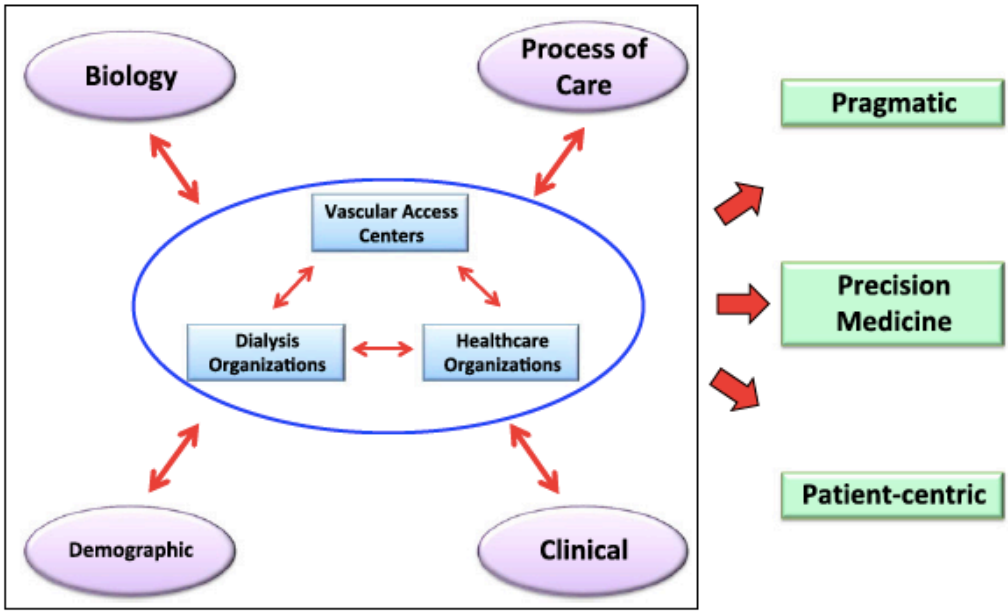


Figure 11 - Precision Medicine Approach to dialysis vascular access

Recommendations for clinical practice:

Nephrologists have a major role in effectively managing patients with chronic kidney disease and facilitating a smooth transition to dialysis and maintenance for those with end stage renal disease. Studies have shown the benefits of AVF as the best vascular access method for hemodialysis (FMC, 2019)

Nephrology office information technology (IT) systems have a great potential to develop a coordinated, progressive, and comprehensive care method for patients with CKD and to ensure an optimal transition to dialysis for patients progressing to ESRD. However, physicians have been reporting frustrations and difficulties with their electronic health records (EHR) system and the transition to electronic health records has been a stressful process. Therefore, the need to advance nephrology office clinical IT systems to an efficient user-friendly system is essential. Providing improved reporting and analytics would enable nephrologists to better manage and coordinate care for all patients with kidney disease. This will help nephrologists to determine the right timing to transition patients to dialysis and provide education regarding the optimal vascular access required for their specific treatment (FMC, 2019).

As a result of these needs, Fresenius Medical Care North America (FMCNA), in collaboration with Epic Systems, has developed Acumen 2.0 as the nephrology office clinical system. Acumen 2.0 has been tailored for nephrology practices, including: (FMC, 2019).

- Providing nephrologists with clinical information at the point of care for best practices
- Reporting and analytics to measure outcomes and population management
- Engaging and managing patients through the patient portal
- Connecting to a national health information exchange platform for improved and tailored care

Recommendations for future research:

Choosing the best vascular access in the appropriate patient, at the correct time and under the given circumstances is challenging. These different alignments depend on several factors that include the patient, facility and administrative specifics. The USRDS data is an important information resource that can provide population-based trends; however, many variables cannot be accounted for in analysis. For example, reducing the percentage of patients initiating HD with a catheter, can only be made at the patient level with patient-specific and unique information (Lok & Foley, 2013).

USRDS does not have the ability to take into consideration critical variables that may affect change. Such examples are patient preferences, expected patient survival or evolvement in clinical practices (e.g. the growing field of interventional nephrology). These changes may affect the quality and cost of care as the indirect and direct costs of complications associated with vascular access is a major focus given the rapid rise is such costs lately. This is necessary especially in the first year of dialysis, when hospitalization and mortality rates are high (Lok & Foley, 2013).

Conclusion

Based upon these finding, future research should provide greater uniformity of the relevant research variables. Studies that include data variables such as hospitalization and health care cost will enhance the ability to provide meaningful change to clinical practice as well as patient and provider education. Improving Electronic Health Records and adding this additional data will be helpful. Effective utilization of EHRs could help in improving both the identification of CKD patients and the quality of care delivered to them. Automated clinical alerts using EHRs may help diagnose CKD earlier and improve

referral rates. There has been promising data that automated estimated glomerular filtration rate (eGFR) reporting in laboratory results improve nephrology referrals. It remains to be seen whether these measures improve patient-centered outcomes (Navaneethan et al., 2013).

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