Evaluation of an Advanced Practice Nurse Led Inter-professional Collaborative Chronic Care Approach for Kidney Transplant Patients: The TARGET Study

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Abstract

The purpose of this study was to evaluate the effectiveness of an Advanced Practice Nurse (APN) led inter-professional collaborative chronic care approach on the achievement of clinical outcomes for adult kidney transplant chronic kidney disease (CKD) patients, as compared to a traditional transplant nephrologist led approach in one Canadian hospital transplant setting.

Methods: In this non-randomized, controlled study guided by the Chronic Care Model (CCM), a propensity-score matched analysis was used to control for confounding variables and potential selection bias. The propensity-score model included the co-variates: a) estimated glomerular filtration rate, b) age, c) sex, d) kidney donor type, and e) diagnosis of diabetes. Based on the CCM elements and CKD clinical practice guidelines, the intervention included strategies for patient disease self-management, end-stage renal disease shared decision-making, healthcare system re-organization, and clinical decision support. The primary outcome was the proportion of patients achieving a target score of 78% (7 out of 9 targets), based on the recommended standards and patient participation in discussions about ESRD options.

Results: Targets included blood pressure, serum lipids, hemoglobin, phosphate, calcium, parathyroid hormone levels, acid-base balance and clinical practice guideline standards. Propensity-score matching of 61 intervention patients to 119 controls, resulted in 40 pairs with an equivalent balance of measured co-variates. Compared to the control group, a greater proportion of intervention patients achieved the target score (68% versus 10%, p=0.0001), participated in end-stage renal disease shared decision-making (88% versus 13%, p=0.0001), and had clinical practice guideline treatments implemented (ASA 50% versus 23%, p=0.01; ACE-I/ARB 53% versus 13%, p=0.004; statins 80% versus 45%, p=0.004). Compared to the intervention group, the control patients experienced a higher incidence of all cause hospital admissions (35 versus 12, IRR 0.34, p=0.02) and emergency department visits (40 versus 21, IRR 0.53, p=0.001).

Conclusions: A CCM based, APN-led approach to care improves both the processes and outcomes of care for kidney transplant CKD patients.

Dedications and Acknowledgements

This thesis is dedicated to those kidney transplant CKD patients struggling and navigating through the myriad of health care system obstacles and decision uncertainties. It is my hope, that as healthcare professionals, we continue to advocate for a health care system that makes your journey less of a struggle, and improves your quality of life. I would also like to dedicate this thesis to the many individuals who supported and listened to my angst over the last five years. My husband Robert, and daughters Elizabeth, Annabelle and Olivia. We sacrificed many opportunities for family time because 'Mom needed to write'. I thank you all, for being so patient and understanding, even though I know you wondered if this was ever going to end..as did I.

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Table of Contents **Page**

Chapter Three

Chapter Four

Chapter Five

List of Figures **Page**

List of Tables **Page**

List of Appendixes **Page**

List of Abbreviations

AOR	Absolute odds ratio
APN	Advanced Practice Nurse
BP	Blood pressure
BPG	Best practice guideline
CBC	Complete blood count
CHF	Congestive Heart Failure
CI	Confidence interval
CIHI	Canadian Institute of Health Information
COPD	Chronic Obstructive Pulmonary Disease
CCM	Chronic Care Model
CKD	Chronic Kidney Disease
CNA	Canadian Nurses Association
CNS	Clinical Nurse Specialist
CPG	Clinical practice guideline
DBP	Diastolic blood pressure
eGFR	Estimated glomerular filtration rate
ES	Effect size
ESA	Erythropoietin stimulating agent
ESRD	End Stage Renal Disease
HbA1c	Glycated Hemoglobin A1c
K/DOQI	Kidney disease outcome quality initiative
IRR	Incidence rate ratio
IUR	Intervention User Rate
M	Mean
Mdn	Median
MDRD	Modification of Diet in Renal Disease
NKF	National Kidney Foundation
NP	Nurse Practitioner
OR	Odds ratio
P	Probability
PCP	Primary care physician
PTH	Parathyroid hormone
RCT	Randomized controlled trial
RNAO	Registered Nurses Association of Ontario
SBP	Systolic blood pressure
U.S.	United States
WHO	World Health Organization

Introduction

Problem Statement

Chronic kidney disease (CKD) affects between 1.9 and 2.3 million Canadians (Levin et al., 2008) and CKD continues to affect up to 60% of patients who progress to end stage renal disease (ESRD) resulting in kidney transplantation (Karthikeyan, Karpinski, Nair, & Knoll, 2003; Marcén et al., 2005). The World Health Organization (WHO, 2002) predicts that by 2020 chronic conditions will contribute to more than 60% of the global burden of disease. Moreover, the most common approaches to health care, which focus on tertiary, episodic or acute health care management do not work when health problems are chronic (WHO, 2002). While kidney transplantation is the treatment of choice for ESRD in terms of prolonged survival (Wolfe et al., 1999), improved quality of life, and is less costly when compared to dialysis (Laupacis et al., 1996), it continues to require chronic disease management.

The traditional or conventional approach to kidney transplant care is one which is led by a specialized transplant nephrologist or surgeon and focuses on the medical management of patients at all stages post transplant. Current studies suggest that kidney transplant patients with CKD in the traditional care approach do not achieve optimal clinical outcomes when compared to non-transplant CKD patients cared for under an inter-professional chronic disease approach (Akbari, Hussain, Karpinski, & Knoll, 2007). Advanced Practice Nurse (APN) led chronic care approaches with inter-professional involvement has been shown to improve patient clinical outcomes and chronic disease self-management skills (Allen et al., 2002, Callahan et al., 2006; Cowan et al., 2006; Litaker, et al., 2003). No studies were found that evaluated the effectiveness of an APN led collaborative chronic care approach for optimizing clinical outcomes in kidney transplant CKD patients. Given the multiple co-morbidities, the complexity of care, and the challenges of chronic disease management for kidney transplant patients with CKD, research is needed to identify

effective approaches to health care to optimize clinical outcomes and patient disease self-management for this subgroup of kidney transplant patients (Akbari et al., 2007; McNatt & Easom, 2000; Gill, Abichandani, Khan, Kausz, & Pereira, 2002).

Conceptual Framework Guiding Chronic Disease Management

The Chronic Care Model (CCM) provides a framework for health care provision across the continuum of chronic disease (Wagner, 1998). The components considered central to effective chronic disease management are community resources, health care organization, health care re-design, self-care management, decision support and clinical information systems (Wagner, 1998). The primary assumption underlying the CCM is that improvement in chronic care requires an approach that integrates patient, provider and health care system interventions. This model was chosen for its focus on patient-centered care, applicability across the spectrum of chronic disease management, and previous use in evaluating the effectiveness of APN roles (Adams et al., 2007; Bodenheimer, Wagner, & Grumbach, 2002; 2002a; Litaker et al., 2003; Watts et al., 2009).

Purpose and Research Questions

The purpose of the TARGET (Targeting Achievement of Renal Goals with Enhanced Care Teams) study was to evaluate the effectiveness of an APN led inter-professional collaborative chronic care approach, guided by the CCM, on achieving clinical targets for kidney transplant CKD patients.

The primary research question was:

1. Is there an association between patients' exposure to the APN led inter-professional collaborative chronic care approach and achievement of clinical targets and discussions about end-stage renal disease options? The hypotheses to be tested were:

- Patients exposed to the APN led inter-professional collaborative chronic care approach are more likely to achieve standardized clinical targets than patients who received traditional transplant clinic care.
- Patients exposed to the APN led inter-professional collaborative chronic care approach are more likely to participate in discussions about ESRD options than are patients receiving traditional transplant clinic care.

The secondary questions were:

2. Is there an association between patients' exposure to the APN led inter-professional collaborative chronic care approach and the number of all cause hospital admissions and emergency department visits? The hypothesis to be tested was:
   - Patients exposed to the APN led inter-professional collaborative chronic care approach have fewer all cause hospital admissions and emergency department visits.
3. Does matching the intervention and retrospective control transplant CKD patients, using the propensity-score method, control for the differences in co-variates between the two groups? The hypotheses to be tested were:
   - The control and intervention groups will be equivalent using the propensity-score method for matching on co-variates as compared to matching on only eGFR.
   - The primary outcome using the eGFR for matching intervention and retrospective control subjects will be different from the results based on alternate propensity-score models.
4. Within the intervention group, is there an association between the number of patients' reported medication non-adherence events and achievement of clinical targets? The hypothesis to be tested was:
   - Patients reporting medication non-adherence events achieve fewer clinical targets as compared to adherent patients.

5. Within the intervention group, is there an association between the chronic disease management dose and patient achievement of clinical targets? The hypothesis to be tested was:
    - Patients achieving clinical targets receive a higher mean dose of chronic disease management intervention as measured by the intervention user rate (IUR).

Chapter One

Literature Review

The literature review was structured to locate and include the practice trends in kidney transplantation and key components of the Chronic Care Model (Wagner, 1998): (a) health care delivery system design (e.g., APN led approach, collaborative practice and case management); (b) disease self-management (e.g., behaviour/adherence change); and (c) decision support (e.g., clinical practice guidelines/protocols and collaborative care). The material included clinical practice guidelines for kidney transplant and CKD, qualitative, quantitative and descriptive studies or reviews on the development and implementation of APN led health care, the Chronic Care Model, collaborative practice, collaborative care and case management. The electronic databases searched for this study included MEDLINE, CINHAL, and PubMed from 1995 to 2009. In addition, the table of contents of recently published journals and the reference lists of included papers were reviewed for relevant publications up to 2009.

This section begins with an overview of chronic kidney disease in kidney transplantation and the recommended clinical practice guidelines. A review of the research related to achievement of clinical practice guideline standards for kidney transplant CKD patients is also described. The literature on APN led approaches to chronic care follows, with specific reference to the RCT and quasi-experimental research results.

Kidney Transplantation: the Ongoing Burden of Chronic Kidney Disease

The Canadian Society of Nephrology defines CKD as the presence of kidney damage for greater than three months, with a glomerular filtration rate (GFR), as a measure of kidney function, less than 60 mL/min/1.73 m² considered abnormal for adults (Levin et al., 2008). End-stage renal disease (ESRD) occurs because of chronic progressive kidney failure and refers to the period just prior to requiring renal replacement therapy in the form of hemodialysis, peritoneal dialysis or

transplantation. Kidney transplantation is the renal replacement treatment of choice because it improves survival rates, quality of life and cost as compared to dialysis (Knoll et al., 2005; Laupacis et al., 1996; Russel et al., 1992; Wolfe et al., 1999). Not all patients with ESRD meet the eligibility criteria for kidney transplantation due to the presence of uncontrolled co-morbidities, such as cardiovascular disease, peripheral vascular disease, active cancer or infection (Knoll et al., 2005).

In Canada, the incidence of ESRD has increased 19% since 1999 with the prevalence rate for renal replacement therapy, in the form of dialysis, rising 43% and a corresponding 45% increase, between 1999 and 2008, in the proportion of people living with a kidney transplant (CIHI, 2010). As of December 2008, there were 21,754 people in Canada receiving dialysis and 14,884 living with a functioning kidney transplant (CIHI, 2010). Kidneys for transplantation can come from either a living or deceased donor. Morbidity and mortality, among pre-transplant and transplant patients with CKD and ESRD, are high as many patients also have cardiovascular disease (CVD) and diabetes (de Mattos et al., 2005; Go et al., 2004). The incidence of CVD in kidney transplant patients is nearly twice that of the general population (de Mattos et al., 2005). In addition, the exposure to immunosuppressive medication is a key component that differentiates the transplant CKD patient population from the non-transplant CKD or ESRD patient population (Gill et al., 2002).

To prevent kidney graft rejection, transplant patients must take a combination of two to three immunosuppressive medications daily for the rest of their lives or the life of their kidney graft. Any reduction or elimination of one or more of these medications puts the patient at potential risk for graft failure and rejection (Morrissey et al., 2005). Studies of medication non-adherence in the kidney transplant population indicate that 15 to 30% of transplant recipients exhibit non-adherence behaviour (Morrissey, Flynn, & Linn, 2007). Immunosuppressive medications, such as

prednisone, cyclosporine, and tacrolimus increase the risk for infection, CVD, cancer, hypertension and diabetes in transplant patients (Curtis, 1992; Kasiske, Guijaro, Masey, Wiederkehr, & Ma, 1996; Sheil, 1996). The potential for these adverse drug side effects creates challenges for patients and healthcare professionals when it comes to balancing the medications' benefit versus risk, and adherence behaviour.

A systematic review of adherence to immunosuppressant therapy after kidney transplant indicated that the odds of graft failure increased seven-fold, from four to 12 percent, in patients who missed, stopped or altered their dose of immunosuppressant therapy without a physician prescription, as compared to those who made no adjustments (Butler et al., 2004). The interventions and behavioural strategies considered to be effective for improving medication adherence include (a) increasing communication and counselling between the patient and healthcare professional, (b) simplifying the medication regimen, (c) involving patients more in their own care, and (d) increasing patient awareness of medication taking behaviour and the risks associated with non-adherence (Hansen, Seifeldin, & Noe, 2007; Laghman-Adham, 2003). The World Health Organization (WHO) suggests that the economic impact of non-adherence on the health care system accounts for billions of dollars in increased health care resources resulting from increased emergency department visits, hospital readmissions, and complication rates (Sabaté, 2003). The patient related consequences include increased mortality, morbidity, and reductions to quality of life (Wilson et al., 2002; Simpson et al., 2006). For the CKD transplant population, adherence can have a major influence on achieving evidence based clinical targets and survival of the transplanted kidney (Butler et al., 2004; Morrissey et al., 2005).

Kidney transplant clinical practice guidelines. The National Kidney Foundation (NKF) Kidney Disease Outcome Quality Initiative (K/DOQI) published the majority of evidence and consensus based clinical practice guidelines (CPG) for patients with CKD, ESRD and kidney

transplant patients (NKF, 2003; 2003a; 2004; 2004a; 2006). The NKF-K/DOQI (2002) task force has also published a five-stage CKD classification schema to aid clinicians in pro-actively screening and identifying CKD-related complications to support early intervention and consequently delay disease progression (see Table 1.1). In addition, the Kidney Disease: Improving Global Outcomes (KDIGO) transplant work group published a more recent update that is specific to the monitoring, management, and treatment of kidney transplant recipients (KDIGO, 2009).

Table 1.1

K/DOQI Chronic Kidney Disease Staging (NKF, 2002)

Stage	Renal Function- eGFR
1	≥90 mL/min/1.73m²
2	60-89 ml/min/1.73m²
3	30–59 ml/min/1.73m²
4	15-29 ml/min/1.73m²
5 (ESRD)	< 15 ml/min/1.73m²

ESRD=end-stage renal disease; eGFR= glomerular filtration rate, calculated using the abbreviated Modification of Diet in Renal Disease Study Equation which is equal to: 186 x (serum creatinine) $^{-1.154}$ x (age) $^{-.203}$ x (0.742 if female) x (1.210 if African American)

In a retrospective study of 1762 non-transplant CKD and kidney transplant CKD patients, followed over a 16-year period, researchers applied the K/DOQI classification to track and compare patients' rate of kidney function decline (Djamali, Kendziorski, Brazy, & Becker, 2003). They found that the rate of decline or disease progression per stage of CKD was significantly slower in the kidney transplant population ($p<0.0001$) as compared to the non-transplant population. In this review, researchers also evaluated the implementation of CKD recommended treatment strategies. Compared to the non-transplant patients with CKD, a lower proportion of kidney transplant CKD patients received guideline recommended treatments (10% versus 25% prescribed erythropoietin treatment for anemia, 25% versus 40% prescribed angiotenson-

converting-enzyme inhibitors or angiotension-receptor blockers for hypertension). The researchers concluded that a more pro-active approach to screening kidney transplant patients for the co-morbid conditions associated with each stage of CKD might improve the implementation of recommended treatment strategies thereby slowing progression of the disease and potentially stabilizing transplant function (Djamali et al., 2003; Becker et al., 2002).

While screening and treating co-morbid conditions are important in maintaining kidney graft function and improving patient outcomes, researchers have evaluated the achievement of CPG recommended clinical targets within each stage of CKD. In a retrospective audit of 4643 transplant patients with progressive CKD, followed under the traditional nephrologist or surgeon led post kidney transplant care, researchers found that 55% and 67% of patients had sub-optimal albumin and hematocrit levels respectively at the time of dialysis initiation (Gill et al., 2002). Similarly, Akbari et al. (2007), in a cross-sectional study compared kidney transplant CKD patients followed under the traditional approach to non-transplant CKD patients under an inter-professional approach to chronic kidney care. In this study kidney transplant CKD patients, as compared to the non-transplant patients, were more likely to have uncontrolled hypertension (AOR 3.8, 95% CI=1.3-10.7), anemia (AOR 6.4, 95% CI= .99-41.9), and dyslipidemia (AOR 4.3, 95% CI=1.4-13.4) (Akbari et al., 2007). Akbari et al. (2007) suggested that a health care approach for kidney transplant patients should include an inter-professional healthcare team. In both studies, the authors concluded that the current approaches to post kidney transplant care fail to optimize clinical targets for patients with kidney transplant CKD and suggested a need to evaluate alternate approaches to optimize clinical targets in the subgroup of kidney transplant CKD patients (Akbari et al., 2007; Gill et al., 2002).

A number of factors can influence target achievement for kidney transplant CKD patients, including the adverse side effects of immunosuppressant medications and the presence of a chronic

inflammatory state (Gill et al., 2002). Moreover, the degree to which specialty physicians in the traditional approach to care implement CKD clinical practice guidelines for kidney transplant CKD patients is unclear; it is also unclear whether opportunities exist to improve the standards of care. Advanced practice nurses were not part of the inter-professional teams in the studies reviewed above. However, there is evidence suggesting that APN supported approaches to care, for patients with chronic disease, improve clinical practice guideline implementation and clinical targets as well as symptom management and patient disease self-management skills (Gabbay et al., 2006; Lee et al., 2007; Litaker et al., 2003; Wagner, 2000), treatment adherence, and team satisfaction (Harwood, Wilson, Heidenheim, & Lindsay, 2004).

In a retrospective audit of 113 CKD patients, researchers measured the effectiveness of a CKD collaborative practice clinic with an APN-NP as compared to a traditional nephrologist led renal/hypertension clinic (Lee, Campoy, Smits, Tran, & Chonchol, 2007). The CKD patient population, in the APN led approach, achieved higher hemoglobin ($p=0.02$), and albumin ($p=0.002$) levels, received more erythropoietin replacement therapy ($p=0.009$), phosphate binders ($p=0.01$), dietary counselling ($p<0.0001$) and dialysis education ($p<0.0001$) as compared to the renal/hypertension clinic patients (Lee et al., 2007). In addition, the renal/hypertension patients had more all cause hospitalizations (86 % versus 51%, $p<0.0001$). In this study, the APN used a standardized protocol based on the K/DOQI clinical practice guidelines to support clinical and treatment decision-making.

In summary, based on the K/DOQI classification guidelines, the prevalence of CKD in kidney transplant patients can be as high as 60% (Djamali et al., 2003; Karthikeyan et al., 2003; Marcén et al., 2005). Early screening and achievement of clinical standards for CKD in kidney transplant patients remains suboptimal. In the above studies, results indicate some evidence in support of APN led care with inter-professional teams as a promising approach for improving outcomes in

primarily CKD patients. However, the retrospective nature of these studies limits the ability to make any clear statements on causality or to generalize these findings to the kidney transplant CKD population. Other studies have demonstrated that the APN, working with an inter-professional team, improves outcomes for a broad spectrum of chronic disease states (Allen et al., 2002; Callahan et al., 2006; Litaker et al., 2003; Naylor et al., 2004). Despite these results, it remains unclear which approach to care best meets the needs of and improves clinical outcomes for kidney transplant patients with CKD. The following section includes a review and discussion of the literature describing the APN role, and the research evaluating implementation of APN led approaches to health care for patients with a chronic disease.

Advanced Practice Nursing (APN)

The provision of care by inter-professional healthcare teams and the addition of APNs working in a collaborative practice environment with physicians are elements commonly found within effective programs of chronic disease management (Lewandowski, 1995; Tsai et al., 2005; WHO, 2002). There is no single definition of APN, but there is agreement that the APN role includes a broadened scope of practice and level of skill (Bryant-Lukosius, DiCenso, Browne, & Pinelli, 2004). The Canadian Nurses Association (CNA) defines APN as "an umbrella term describing an advanced level of clinical nursing practice that maximizes the use of graduate educational preparation, in-depth nursing knowledge and expertise in meeting the health needs of individuals, families, groups, communities and populations. It involves analyzing and synthesizing knowledge; understanding, interpreting and applying nursing theory and research; and developing and advancing nursing knowledge and the profession as a whole." (CNA, 2008, p 10). The CNA recognizes both the masters prepared clinical nurse specialist (CNS) and nurse practitioner (NP) roles as APN positions.

As health care needs evolve, in the context of rising costs, an aging population, and the associated increase in chronic disease prevalence, so has the presence and demand for APNs beyond the acute care setting to primary, chronic, ambulatory, and community care settings (Bryant-Lukosius et al., 2004). Evidence about the benefits of advanced practice nurses on patient outcomes continues to build. Fulton and Baldwin (2004) in a review of 70 research papers examining the impact of clinical nurse specialists found a reduction in emergency department visits among asthma patients and fewer complications among cancer patients when care teams included a CNS. Kleinpell (2007) reported that the use of APNs in the acute care setting decreased readmissions for heart failure, shortened lengths of stay for re-admissions and lowered rates of urinary tract infections, skin breakdown and pneumonia among patients. Despite the increase in published research evaluating the effectiveness of APNs, there continues to be a need for more research on the results of specific APN led approaches to health care to improve our knowledge and understanding of the impact in other chronic disease and health care settings (Oerman & Floyd, 2002).

APN led approaches to health care. The growing evidence demonstrating the benefits of APN led health care across diverse health care settings and the need to optimize patient disease self-management and outcomes for those with chronic disease provided the basis upon which to investigate the potential benefit of an APN led approach to care for kidney transplant CKD patients. This literature review focused on studies which included an APN supported or led approach to health care, for patients with a chronic disease in order to identify an evidence-based approach to implementation and a theoretical framework best suited to guiding care for kidney transplant CKD patients. The search and selection process included studies, published between 1998 and 2009, which involved adults with chronic disease, and focused on the evaluation of an APN led or integrated chronic disease focus of care. The databases searched were the Cochrane

Database of Systematic Reviews, Medline, CINAHL, PsychINFO, and EMBASE. In addition, tables of contents of the journals most frequently identified in the electronic search were reviewed (Journal of Advanced Nursing, Journal of Nursing Administration, Disease Management, and Journal of the American Medical Association); reference lists of retrieved papers were also scanned for relevant studies.

Twelve studies, in which the APN was a member of the healthcare team for patients with a chronic disease, were identified (see Appendix I). Of the 12 studies, six were randomized controlled trials (RCT) and six involved quasi-experimental methodologies with either (a) a pre-post intervention design (n=1), (b) a retrospective two-group comparative review (n=2), or (c) a prospective comparative review (n=3).

Randomized controlled trials of APN led approaches to health care. In the six RCT studies, researchers compared a chronic disease management approach that included an APN to usual care. The researchers evaluated the effectiveness of the APN led care based on specific clinical, quality, or functional outcomes of care for patients with a range of chronic conditions. These conditions included cerebral vascular disease (Allen et al., 2002), diabetes (Litaker et al., 2003; Wong et al., 2005), Alzheimer's disease (Callahan et al., 2006), or heart failure (Naylor et al., 1999; 2004). The total number of patients included in these RCTs was 1,004, with 504 randomized to the interventions and 500 to usual care. No RCT studies that evaluated the effectiveness of an APN led approach to healthcare for patients with CKD or kidney transplantation were located.

In the two largest RCTs, Naylor and colleagues (1999; 2004) evaluated the effectiveness of an APN led transitional healthcare approach, which included a directed discharge protocol for patients with heart failure transitioning from the acute care setting to home. In both studies, there were significantly reduced re-hospitalization rates in the intervention groups as measured by (a) time to readmission (p=0.03), (b) re-admissions at 52 weeks (105 versus 162, p=0.05), and (c) re-

hospitalizations related to co-morbid conditions ($p<0.01$) (Naylor et al., 1999; 2004). Naylor et al. (2004) also did an economic evaluation to determine the savings associated with a reduction in re-admission rates and found that the cost of care was significantly lower in the intervention group (US$7, 636 versus US$12, 481, $p=0.002$). No differences were found between the two groups in the post intervention functional status measures in either study. The authors suggested that three main factors influenced the success of the APN led transitional health care approach: (a) Continuity of care as provided by the APN, (b) the use of a directed discharge protocol, and (c) the APNs use of a holistic expertise-based, collaborative approach to address the patient's complex needs (Naylor et al., 2004).

Similarly, Wong and colleagues (2005) evaluated the effect of an APN led approach for the healthcare of diabetic patients transitioning from the acute care setting to home. The effect of an APN initiated, early discharge protocol on glycemic control for diabetic patients (n=52) admitted to an acute care setting was compared to a usual care group (n=49) followed by the primary care physician and discharged based on the physician's clinical judgement. Both groups received diabetic counselling and education during their inpatient stay although the intervention group received this education from the APN as compared to a diabetic nurse specialist for the control group. The authors did not describe the diabetic nurse specialist, in this manuscript, as being in an APN role.

The post discharge care included a follow-up telephone call by the APN, to the intervention patients to review their glycemic levels, assess their adherence with the self-monitoring of glucose levels, and their medication taking behaviour. The APN adjusted the patients' glucose-controlling medications based on a pre-established clinical protocol and the patients' glucose levels. Both groups had follow-up clinic appointments at 12 and 24 weeks post discharge. The patients in the control group met with their primary care physician, whereas the APN-physician team saw the

intervention patients. Intervention patients had significantly higher levels of blood glucose monitoring ($p<0.001$) and exercise adherence ($p<0.001$), as well as a greater improvement in HbAIc (7.6% versus 8.1%, $p=0.06$) compared with the controls. In addition, the length of hospital stay was significantly lower in the intervention patients, with a mean difference between groups of 3.7 days ($p<0.001$). No significant difference was found between the groups, in medication adherence, body weight, or frequency of hospital readmission (Wong et al., 2005). Wong et al. (2005) suggested that an APN led transitional and chronic care approach stabilizes diabetic patients' glycemic control. Wong, as had Naylor and colleagues (1999; 2004), suggested that the healthcare approach's success was in part due to features of the intervention, which incorporated comprehensiveness, continuity, coordination and collaboration between the healthcare professionals (Wong et al., 2005).

In the remaining three RCTs, an APN led chronic disease management care approach in the outpatient settings was compared to usual care provided by the patient's primary care physician. The chronic disease and APN intervention in each study was different and included (a) APN-care management for stroke patients (Allen et al., 2002), (b) an APN in collaboration with the physician and an interdisciplinary team for patients with Alzheimer's disease (Callahan et al., 2006), and (c) APN-physician collaborative care for patients with hypertension and diabetes (Litaker et al., 2003). A common feature of the APN interventions, within each study, was the use of a standardized clinical protocol to guide the APN's treatment decision making. In the first study, the APN used a standardized bio-psychosocial assessment with the stroke patient population, to identify stroke related problems and then developed a care plan in consultation with the interdisciplinary team and physician based on the findings (Allen et al., 2002). In this study, there was a significant ($p<0.0001$) improvement in the intervention patients' profile of health and prevention ($n=47$). There was also a significant effect size for five measured health domains in the intervention group

as compared to the control group (n=46) who received usual care by their primary care physician. These health domains included neuro-motor function (0.1, 90% CI=-0.3 to 0.5), severe complications (0.4, 90% CI=0.1 to 0.8), quality of life (0.5, 90% CI=0.1 to 0.9), management of risk (0.6, 90% CI=0.3 to 0.1), and patient stroke knowledge (1.0, 90% CI=0.6 to 1.4).

In the second study, researchers compared APN-physician collaborative practice to the usual care provided by the primary care physician for patients with Alzheimer's disease (Callahan et al., 2006). As in the prior studies, the APN used standardized protocols for the initiation of evidence-based treatments. The APNs who had expertise in geriatrics were the case managers and assessed the patients in the clinic bimonthly, then monthly for 12 months. At these clinic visits, the APN completed a memory and behaviour problems checklist that triggered either a non-pharmacological or a pharmacological intervention. The APN initiated at least one protocol which was triggered based on the assessment findings in 89% (n=84) of patients. The intervention patients were more likely to receive cholinesterase inhibitors (79.8% versus 27.5%, p=0.03) and less likely to experience behavioural psychological symptoms of dementia (p=0.01), as compared to the control group (n=69) (Callahan et al., 2006).

The third and final RCT by Litaker and colleagues (2003) compared physician only care to NP-physician team based care for patients with hypertension and diabetes. A key element in this intervention was the focus on chronic disease management within the NP-physician approach, again using clinical practice algorithms, in addition to patient education on disease self-management strategies. The intervention patients received regular monitoring and feedback by telephone or during clinic visits by the NP, as first line contact. As compared to usual care (n=78), patients who received care within the NP-physician approach (n=79) improved their diabetes control and lipid profile with a mean change in HbA1c of -0.7% (p=.02) and high-density

lipoprotein of +2.6 mg/dL (p=0.02) (Litaker et al., 2003). Moreover, in the intervention arm of the study, patient satisfaction with care increased significantly (+6.2 versus -1.7, p=0.01).

In summary, all RCT studies of APN led care reported similar findings. The implementation of an APN role with a collaborative chronic disease focused approach to health care significantly reduced re-hospitalization rates for patients with congestive heart failure (Naylor et al., 2004), increased blood glucose monitoring and exercise adherence among patients with diabetes (Wong et al., 2005), and increased the use of cholinesterase inhibitors for patients with Alzheimer's disease (Callahan et al., 2006). The authors suggested that key components were necessary for the success of an APN-led health care approach. These components were (a) the use of an inter-professional healthcare team, (b) the use of evidence-based practice protocols, (c) increased patient participation in disease self-management, (d) an emphasis on patient education, (e) collaboration between members of the healthcare team, and (e) the APN as case manager to enhance the coordination and continuity of patient care. Some common limitations noted within these RCTs were the small sample sizes, short follow-up periods, and inadequate reporting to determine the dose of interventions. The researchers described the interventions in detail, but did not provide a measurement of the amount, frequency, or duration of the intervention, which may limit replication or generalization of these study results.

Quasi-experimental studies of APN led approaches to health care. In two retrospective studies, researchers compared APN led care to usual care for patients with chronic or end-stage renal disease (Harwood et al., 2004; Lee et al., 2007). In the Harwood et al. (2004) retrospective cross-sectional review of 112 hemodialysis patients, researchers evaluated the influence of NP-CNS and nephrologist collaborative practice on patient outcomes. The key process of care interventions implemented by the NP-CNS included (a) coordination of patient services, (b) continuity of care, (c) patient education and care discussions, (d) promptness in addressing team

members' concerns regarding patient care, and (e) prevention and early intervention for co-morbidities or complications. The NP-CNS used medical directives derived from the K/DOQI to guide treatment decisions. As compared to the nephrologist only led care, the health care team members within the NP-CNS led care reported significantly greater team satisfaction and perceptions of care delivery (i.e., team members perceived the quality of care to be better than that provided by the nephrologist only led care, $p<0.0001$). As compared to the patients receiving the nephrologist led care, a significantly greater proportion of patients followed by the NP-CNS received evidence-based treatment standards (i.e., adjustments to target weights and medications, $p<0.004$). There were no differences between the two groups in clinical outcomes, such as weight gain between dialysis sessions, frequency of blood transfusions, emergency department visits or admissions to hospital over the last three months of the study.

The authors noted that the group of patients cared for within the collaborative care approach had significantly more co-morbidities than the usual care group, which could in part account for the lack of significant difference in patient outcomes. The authors concluded that the patient outcomes in the collaborative practice approach were as good as those in patients cared for by the nephrologist only, yet suggest a future study that controls for co-morbidities may come to a different conclusion. Moreover, the authors suggest that involving APNs in collaboration with nephrologists, to address some of the day-to-day stable clinical and chronic disease management issues for dialysis patients does not compromise care. Moreover, this may allow the nephrologist additional time to address acute care issues outside the APNs scope of practice (Harwood et al., 2004).

In the second retrospective study, outcomes for patients with CKD followed by an APN-NP and nephrologist collaborative practice team were compared to those for patients cared for in a renal hypertension clinic by nephrologists in training under the supervision of board certified

nephrologists (Lee et al., 2007). The chart audit included 113 patients seen consecutively in either clinic over 12 months. In the APN-NP clinic, standardized K/DOQI based protocols were used to support treatment decisions. These clinic patients more often met hemoglobin and albumin targets ($p<0.02$), more often received erythropoietin replacement therapy ($p=0.009$), phosphate binders ($p=0.01$), dietary counselling ($p<0.0001$), and dialysis education ($p<0.0001$) as compared to the renal hypertension clinic group. Patients in the renal hypertension clinic had a significantly greater decrease in diastolic blood pressure (7.1 versus 1.5 mmHg, $p=0.04$). No significant difference was found between groups in all-cause mortality ($p=0.52$). The authors suggested that a clinic for patients with CKD, with dedicated staff focused on meeting K/DOQI guidelines, might help streamline routine care and improve the implementation of recommended practice standards (Lee et al., 2007).

The sample sizes were small for both these studies and significant differences existed in the baseline clinical characteristics (i.e., prevalence of diabetes, ischemic heart disease, eGFR, and sex) between patient groups. The use of standardized protocols and the APN role were common to both studies. It appears likely that the use of formal protocols combined with the APN role and scope of practice, as compared to a consensus approach to clinical decision-making, may increase the proportion of CKD patients achieving the recommended standardized clinical targets for CKD.

In the final group of four quasi-experimental studies, researchers evaluated the impact of APN led health care using a pre-post intervention design (n=1) or a non-equivalent control group design (n=3). The pre-post intervention study was an audit to evaluate the quality of process of care measures (e.g., implementation of clinical practice guidelines for hypertension and diabetes management) and outcomes for patients with diabetes (n=211), and hypertension (n=541) who received care from collaborative practice teams led by an APN (Graham et al., 2006). The recruitment of study participants was from four primary health care sites. Patients with diabetes

and hypertension were 1.82 ($p<0.05$) and 2.73 times ($p<0.001$) respectively more likely, post intervention, to achieve blood pressure targets respectively, and to be screened for co-morbidities such as nephropathy and hyperlipidemia. No improvements in self-management education indicators for patients with diabetes (e.g., home glucose monitoring) were found.

A limitation associated with this study is the potential Hawthorne effect, as the healthcare professionals were aware of the study focus and the research questions (Graham et al., 2006). This may have increased the healthcare professional's attentiveness to the implementation of recommended practice standards for patients with diabetes and hypertension. In addition, improvements observed post-implementation may be due to improved clarity of documentation rather than an actual improvement in patient care. The authors also described missing or inaccurate data and incomplete documentation as a limitation. Despite these limitations, a change in practice patterns, involving the implementation of an APN and collaborative practice team, to enhance chronic disease care, may have resulted in improved outcomes for patients with diabetes and hypertension. These results again are similar to the earlier study's findings where authors suggest that APNs working in a collaborative practice environment enhance outcomes for patients with chronic disease (Graham et al., 2006; Harwood et al., 2004; Lee et al., 2007).

In the remaining three quasi-experimental studies, researchers compared APN led chronic care to usual care. Vrijhoef and colleagues (2001) examined APN led care in the primary care setting and compared it to usual care for patients with chronic obstructive pulmonary disease and diabetes. In this study, stable type II diabetes patients participated in three, quarterly consultation visits with an APN who focused on interventions to improve the patient's glycemic control using a protocol for treatment decisions (Vrijhoef et al., 2001). A significant improvement was found for glycemic control (8.6% to 8.3%, $p= 0.001$) in the intervention group ($n=52$) as compared to a non-equivalent control group ($n=47$) for whom usual care was provided by an internist.

In the second study, with a non-randomized convenience sample, researchers compared an APN directed transitional home care approach for COPD patients (n=41) to usual home care by an RN or Licensed Practical Nurse (n=39) (Felber-Neff et al., 2003). The comparison in this study differed from many APN led health care evaluations in which the control is more likely to be a physician led approach. The intervention in this study included (a) APN directed home visits for teaching and assessment of complex care needs, (b) patient telephone contact and follow-up by the APN, and (c) APN consultation with the primary care physician for patients identified as high risk. Significant reductions in re-hospitalization and acute care visits ($p<0.05$) were found in the intervention group, with no differences found between the groups in dyspnea scores post intervention. In both studies, the sample sizes were small and groups differed on baseline characteristics such as sex, age and presence of co-morbid conditions. It is therefore difficult to attribute any cause and effect relationship based on the intervention alone.

Summary

Kidney transplant CKD is a chronic disease with complex causes, manifestations, complications, and management challenges. The prevalence of CKD in kidney transplant patients is estimated to be as high as 60%, yet when compared to non-kidney transplant patients with CKD, the rate of disease progression is significantly slower (Djamali et al., 2003). Along with the increased prevalence, comes the additional need to optimize health care and patient outcomes for the multiple co-morbidities associated with CKD. However, the slower progression of CKD provides a greater opportunity for the screening for co-morbidities and optimizing implementation of CKD practice standards (Gill et al., 2002). In studies where an APN led chronic care approach is compared to usual care for patients across a variety of chronic disease conditions and health care settings, results consistently show optimization of patient outcomes and improved implementation of evidence-based standards of care. Combining the knowledge and expertise of the APN, in

collaboration with the physician and an inter-professional healthcare team, guided by a chronic care focus, may be a feasible approach to improve outcomes for kidney transplant patients with CKD.

Chapter Two

Evidence Review to Support a New Kidney Transplant CKD Care Approach

This chapter includes an overview of the research and literature on the Chronic Care Model (CCM) (Wagner, 2000) and its use as a conceptual framework to support implementation and evaluation of the APN led inter-professional collaborative care approach for kidney transplant CKD patients. The literature review included the key terms chronic care model and chronic care framework. The electronic databases searched included MEDLINE, CINHAL, and PubMed from 1995 to 2009. In addition, the table of contents of recently published journals and the reference lists of included papers were reviewed for relevant publications up to 2009.

The chapter begins with a description of the Chronic Care Model, followed by a new conceptual framework adapted from the model. A review of the evidence of the effectiveness of the CCM provides the background to an outline of the models structure components and measures of quality. The final section describes and defines each of the key elements of the CCM, again with the evidence supporting implementation of these elements to enhance patient outcomes in chronic disease management.

The Chronic Care Model

Wagner (1998) originally developed the CCM as a generic framework to guide the provision of health care for primary care patients with a chronic illness. Because nearly 90% of the chronically ill are treated in the primary care setting, the CCM represents a re-organization of primary health care delivery (Bodenheimer, Lorig, Holman, & Grumbach, 2007; Coleman, Austin, Brach, & Wagner, 2009; Nutting et al., 2007). Through this re-organization of care delivery, a new environment is created, that shifts the healthcare professionals' focus to a patient engaged, pro-active and planned chronic disease management approach to health care (Bodenheimer et al., 2007;

Coleman et al., 2009). The CCM outlines and organizes the changes needed in the health care system, the practice, and the patient to improve outcomes (Wagner et al., 2001). Although the model does not offer a quick fix to the primary healthcare system, it is a multidimensional solution to the very complex problem of chronic disease management (Bodenheimer et al., 2002). Wagner et al. (2001) intended for the CCM to be generic in nature, making it applicable to multiple chronic diseases and health care organizations. The CCM was chosen as the framework to guide the evaluation of this study due to its focus on patient-centred care, applicability across the spectrum of chronic disease management, and use in evaluating the effectiveness of APN roles (Adams et al., 2007; Litaker et al., 2003; Watts et al., 2009).

The shift to a chronic care approach is accomplished by integrating key elements of the CCM that are specifically designed to improve the patient-healthcare professional relationship and health outcomes (Coleman et al., 2009). These elements are (a) organizational support, (b) the optimization of community resources or linkages, (c) disease self-management support, (e) integrated decision support, (f) delivery system re-design, and (g) the use of clinical information systems (Bodenheimer et al., 2002; 2002a). The improvement in quality of health care outcomes, which researchers suggest occurs with the implementation of the CCM, is believed to be due to the integration of the above components although, as of this time, there is not enough evidence to indicate which component, if any, is the most important (Adams et al., 2007; Bodenheimer et al., 2007; Callahan et al., 2006). Based on the CCM, quality health care outcomes in chronic disease management could include such measures as (a) reductions in re-admission rates or delay to re-admission, (b) reduction in health care costs, (c) improved symptom management, (e) increased use of patient disease self management strategies (e.g., home glucose and blood pressure monitoring), and (e) optimization of disease specific clinical outcomes (e.g., HbA1c, blood pressure, and lipid profiles) (Bodenheimer et al., 2002; 2002a; Nutting et al., 2007; Wagner, 2000).

Wagner and colleagues (2001) suggest that in order for the CCM to be effective, it must also integrate the three overlapping sectors of (a) the community, (b) the health care system, and (c) the healthcare provider organization. According to Donabedian (2005), also examining the process of health care helps determine whether what we know to be effective care, based on recommended practice standards, is actually, what is applied in practice. Primary outcome analysis should not be the sole approach to evaluating an intervention's effectiveness (Donabedian, 2005). By broadening the evaluation to include structure and process measures, the objective shifts to answering the broader question about; 'What goes on here?' rather than 'What is wrong, and how can it be made better?' (Donabedian, 2005). This then allows for a clearer understanding of the changes that have been made that may drive changes in the outcomes. The measures of quality in health care should include the actual care provided (i.e., process), actual care received (i.e., outcome) and the capacity of the healthcare professionals to provide evidence-based care (i.e., structure).

For this study, the CCM framework was adapted to form a new conceptual framework, which included structure, process, and outcomes to guide a broader evaluation of an APN led inter-professional collaborative approach to care for kidney transplant patients with CKD. Each component of the CCM encompasses a wide variety of chronic disease management focused supportive structures (i.e., APN-physician collaborative practice environment, collaborative patient care, evidence based care, and accessible information systems). The processes are the recommended practice standards (i.e., use of protocol-based clinical decision support, inter-professional healthcare teams) and patient centred interventions (i.e., case management, behaviour change) which optimize patient engagement at the point of care (see Figure 2.1). In the following section the evidence of the effectiveness of the CCM is reviewed with particular reference to the elements that influence implementation of a chronic care approach to healthcare.

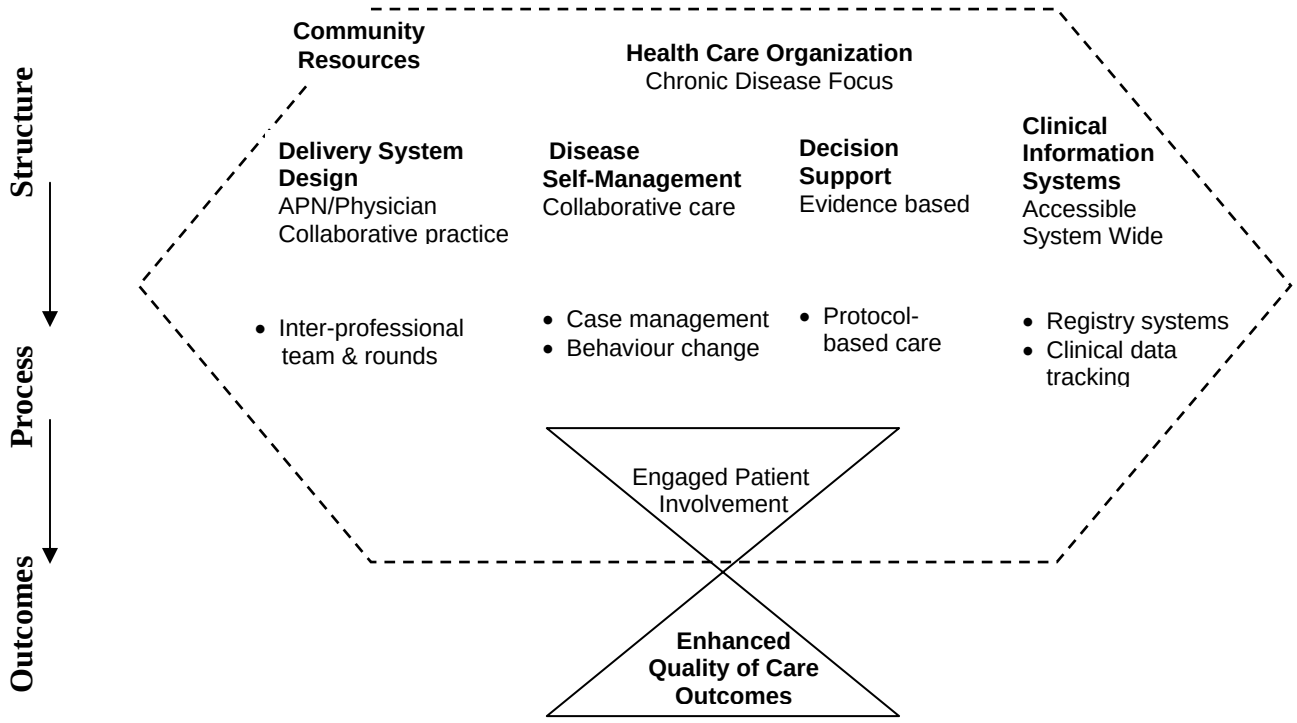

Figure 2.1

An APN led inter-professional collaborative chronic care approach for kidney transplant CKD patients. (Adapted from Wagner et al., 2001)

Evidence of the effectiveness of the CCM. In a systematic review of 39 randomized controlled trials, evaluating the effectiveness of the CCM, it was demonstrated that interventions based on the CCM elements or its components (a) improved at least one process or outcome measure for diabetic patients, and (b) reduced health care costs or lowered the use of health care services for patients with asthma, diabetes, and congestive heart failure (Bodenheimer et al., 2002; 2002a; Wagner & Grumbach, 2002a). Similarly, in a review of 20 RCTs to determine the influence of the CCM or its components on clinical outcomes for patients with chronic obstructive pulmonary disease, disease self-management knowledge significantly improved in the intervention group in the four RCTs in which self-management knowledge was measured (Adams et al., 2007).

The pooled results of 3 of the 20 RCTs that used the Borg scale as a standard for measuring dyspnea indicated a significant improvement in dyspnea (mean change, -0.63, [95% CI], [-1.09 to -0.18]). In addition, the pooled results of another 3 RCTs that implemented multiple CCM components and reported emergency department visits, showed a significant reduction in these visits (RR, [95% CI], 0.58 [0.42-0.79]) in the intervention groups when compared to controls (Adams et al., 2007). The researchers suggest that an effective strategy to improve outcomes for patients with chronic obstructive pulmonary disease is to incorporate two or more of the CCM components in the model of care. The CCM components most commonly combined within these RCTs included (a) nurse supported patient-focused disease self-management skills enhancement, (b) clinical decision support through evidence-based protocols, and (c) ongoing communication and collaboration between the nurse and primary care physician (Adams et al., 2007; Bodenheimer et al., 2002a).

Although the evidence indicates that the CCM is effective as a framework to shift disease management to a focus on the continuum of chronic disease, there remains a need to evaluate the uptake of specific processes into the practice standards of healthcare professionals (Adams et al., 2007; Coleman et al., 2009; Kreindler, 2009; Nutting et al., 2007). Clearly defining the process and outcome measures associated with the six key CCM structural components (e.g., community resources, health system organization, delivery system design, disease self-management, decision support, and clinical information systems) is one approach for guiding the evaluation of both the implementation and uptake of practice standards (Donabedian, 2005; Wagner et al., 2001). Table 2.1 provides an analysis and synthesis of these elements in relation to the process and outcome measures of quality.

Table 2.1

Chronic Care Model Structure Components and Measures of Quality

Model Structure	**Measures of Quality**		
	Process		Outcomes
Community Resources	Availability/ accessibility of community and referral sources.	• pro-active patient screening for community/referral source need • feedback to/from other healthcare provider services	• number of referrals • partnerships with community organizations/health care services
Health System Organization	Chronic disease focus.	• organizational and administrative support • supports quality improvement	• space/resources to provide care based on patient growth
Delivery System Design	Collaborative practice. Qualifications of healthcare professionals.	• APN/Physician collaboration • inter-professional healthcare team • policies outlining scope/ practice standards for healthcare team • patient focused team rounds	• staff/patient satisfaction • clinic appointments pre-scheduled for regular follow-up
Disease Self-Management	APN led model of care. Patient centered care. Collaborative patient care.	• case management • continuity of care • holistic health care focus • pro-active health screening • motivational interviewing • actively engaging patient: goal setting, enhancing self-efficacy	• behaviour change • patient knowledge • symptom control • treatment adherence • disease specific clinical outcomes • referral to education sessions
Decision Support	Access to and existence of evidence based standards.	• standards of care applied in practice • healthcare professional participation in continuing education	• % patients receiving recommended standard • % patients achieving recommended clinical target
Clinical Information Systems	Access to reminder/ clinical tracking systems.	• patient registry/clinical data systems • automated/paper based reminder systems	• hospital re-admission rates • healthcare service use

The following provides an outline the relationship between each of the model structure components with the process and outcome measures. For example, the process of pro-actively

screening patients for community health care needs such as inadequate knowledge for diabetes management provides an integrated link to the CCM structural component of community resources. The actual number of referrals or established partnerships with community organizations is an objective measure of the integration of screening for and referral to the community resource. The APN-physician and inter-professional team collaborative practice environment is a health care delivery system re-design. The development and availability of existing policies outlining the scope and practice standards for each professional, is a process that increases the success of a collaborative practice teams influence on enhancing patient outcomes (Nugent & Lambert, 1996; Zwarenstein & Reeves, 2006). Staff and patient satisfaction are the measurable outcomes of a collaborative practice health care environment (Harward et al., 2004; Litaker et al., 2003).

The integration of the key structural elements of the chronic care model is an important aspect of optimizing patient outcomes. These elements include community resources, health system organization, delivery system design, disease self-management strategies, decision support, and clinical information systems. Each of these supporting elements are reviewed in the following section.

Community resources. Community resources can expand the capacity of a health care system to support individuals with chronic conditions. Early identification of patients with unmet non-health needs, such as housing or social support, can reduce the use of health care services as these needs influence an individual's ability to cope with chronic disease on a long-term basis (Wagner et al., 2001). A partnership with local community centers, health services, diabetes education programs, seniors programs, weight management programs, and/or national patient organizations can supplement the health professional's care for chronically ill patients (Bodenheimer et al, 2002). In general, these programs are able to provide social support, education, and care at a

broader community based level. The community programs best suited to the kidney transplant and CKD patient's disease self-management needs include The Kidney Foundation of Canada, Canadian Diabetes Association, Heart and Stroke Foundation, and the Lung Association. These community partners provide patients, their families and friends with additional opportunities for disease self-management support, educational resources, social support groups, counselling, exercise programs, and smoking cessation programs.

A significant cause of ESRD and co-morbidity in the kidney transplant CKD population is diabetes (Levin et al., 2008). Community diabetes interventions generally occur outside the typical transplant clinic setting. Individuals access these programs primarily through a consultation process initiated by their kidney transplant healthcare professional. The lifelong medication regimen of kidney transplant CKD patients predisposes them to the development or worsening of diabetes (Kasiske et al., 1996; Go et al., 2004). The formalization of referrals and a consultation partnership between the transplant clinic and local diabetic education centres may help to ensure the tailoring of diabetes care to the unique needs of the kidney transplant patient.

Healthcare organization. Leadership within the healthcare organization, be it the primary or acute care setting, plays an important role in system wide improvements by demonstrating commitment to a chronic care disease focus, supporting changes to improve the implementation and standardization of best practices, and development of performance measures reflective of quality in chronic patient care (Wagner et al., 2001; Kreindler, 2009). Support and guidance from administrators at the organizational level is important for influencing change (Stetler, 2003; Ploeg, Davies, Edwards, Gifford, & Elliot-Miller, 2007). A review of the nursing literature on the barriers and facilitators to use of nursing best practice guidelines identified leadership, at all levels of the organization, as key to successful guideline implementation (Ploeg et al., 2007). Preconditions identified as facilitating a system wide improvement include staff involvement prior

to implementation, sufficient time and resources for implementation, clear goals, and the use of evaluation results to inform decisions (Kreindler, 2009). However, within the context of the CCM, the effect of the healthcare organization and leadership on chronic care outcomes remains unclear.

Key to the success of the implementation of APN roles is the existence of organizational and administrative support, resources, and a commitment to the value APNs provide to the organization and to patients (CNA, 2008). The issues found to negatively influence the introduction of an APN role into an organization include (a) confusion about the APN title, (b) failure to clearly define the role and scope of practice within the working environment, (c) role emphasis on physician approval of all APN treatment decisions, (d) underutilization of all APN domains of practice, (e) failure to recognize factors that undermine the role, and (f) limited use of evidence-based approaches to guide implementation (Bryant-Lukosius, DiCenso, Browne, & Pinelli, 2004). In the PEPPA framework (participatory, evidence-based, patient-focused process for APN role development, implementation, and evaluation), the first step in implementing the APN role is defining a specific patient population and examining the existing approach to care (Bryant-Lukosius & DiCenso, 2004). The next step is to consult with stakeholders for involvement in any potential organization of care changes and a reflection on whether a change is truly required. The stakeholders then identify the key challenges and set goals, and clearly define the APN role within the new approach to care. The final steps involve planning the implementation, initiating the APN role, and evaluating the role and care approach at an initial phase, in addition to a long- term monitoring and evaluation process (Bryant-Lukosius & DiCenso, 2004). A structured approach to implementation and evaluation of a new APN supported care approach enables the integration of changes, based on those areas identified as key challenges, to further enhance patient outcomes and improve quality of care (Oermann & Floyd, 2002).

Healthcare delivery system design. The identification of the particular types of healthcare patients need and a re-clarification of the healthcare professional roles based on these needs are required in order to reorganize the healthcare delivery system. Each healthcare professional requires defined roles and objectives, with dedicated time to assess the patient, develop a plan of action, and collaborate with other healthcare team members. Collaborative practice between healthcare professionals is an interaction that focuses, not only on the quality of chronic disease management and patient outcomes, but also on the development of a collegial relationship that enhances professionalism and mutual understanding (Neale, 1999).

Collaborative practice. Collaborative practice is part of the health care system re-design within the CCM. Collaboration in this context refers to the interaction and relationship between members of the inter-professional care team. Martin and colleagues (2005) define collaboration as the independent association or day-to-day interaction of healthcare professionals including nurses, physicians, pharmacists, dietitians, social workers, and other professionals, all committed to the common goal of providing and supporting patient care. In a chronic disease management model, the common goal is to pro-actively support and enhance patient disease self-management. Factors positively influencing the success of a collaborative practice environment include (a) the use of open communication between healthcare professionals, (b) shared authority, and (c) a common philosophy of care (Nugent & Lambert, 1996). Barriers to collaborative practice include (a) the existence of traditional values in terms of the expected scope of practice for nurses, as compared to physicians, and (b) the lack of inter-disciplinary education as a means of improving understanding of role differences (Nugent & Lambert, 1996). Arcangelo and colleagues (1996) suggest that the maintenance of effective collaboration between healthcare practitioners depends on trust, knowledge, shared responsibility, and mutual respect.

A Cochrane Collaboration systematic review of practice-based interventions, designed to improve inter-professional collaboration, identified five RCTs; two examined inter-professional rounds, two examined inter-professional meetings, and one study examined an externally facilitated inter-professional audit as compared to no or an alternate intervention (Zwarenstein, Goldman, & Reeves, 2009). In the two studies examining inter-professional rounds on patient outcomes, one found that daily inter-professional rounds on inpatient medical wards (n=567), compared with traditional physician/resident rounds (n=535), reduced the mean length of stay (5.46 versus 6.06, p=0.006) and mean cost (US$6,681.00 versus US$8,090.00, p=0.002). The second RCT, examining inter-professional meetings to enhance collaboration, found that the implementation of monthly meetings in 15 nursing homes, after 12 months, reduced the use of non-recommended hypnotics (37% versus 3%, $p < 0.001$) and antidepressants (59% versus 34%, $p<0.002$).

Of the five studies reviewed, authors rated only the RCT examining inter-professional monthly rounds on the quantity of psychotropic drug prescribing in nursing homes as 'high quality' and the remaining four as 'moderate quality'. The studies found to be of moderate quality had limitations related to differences between groups in patient baseline characteristics, potential contamination of the interventions through use of the same team members, lack of reporting on numbers of providers for satisfaction survey responses, or lack of information on patient level outcomes. The authors concluded that practice-based interventions aimed at improving inter-professional collaboration through practice changes might improve health care and patient outcomes. However, the authors caution that results based on this small number of studies, be considered promising as opposed to proven (Zwarenstein, Goldman, & Reeves, 2009).

Fourteen intervention studies, published between 1955 and 2001, were identified in an earlier systematic review evaluating inter-professional, collaborative practice (Zwarenstein & Reeves,

2006). The results in nine of these intervention studies indicated that there was a positive impact when interventions were implemented within an inter-professional collaborative practice environment. The authors concluded, despite the heterogeneity of studies in this review, that good inter-professional collaboration might facilitate evidence-based practice through a variety of mechanisms. These mechanisms include (a) effective communication between professionals about patient needs, (b) identification and correction by the professional when evidence-based practice is not followed, and (c) implementation of evidence-based practice recommendations in the practice setting. In contrast, poor collaboration among health professionals was suggested to reduce the potential for evidence-based practice through a lack of the above mechanisms (Zwarenstein et al., 2006). The authors concluded that further research is required to provide a more rigorous insight into the influence of inter-professional education on collaboration and outcomes of care.

In summary, research on the influence of collaborative practice environments on patient outcomes remains limited however, there is evidence that poor inter-professional collaboration can have negative effects on health care. In one U.S. sentinel event alert, of infant death and injury during delivery, inter-professional communication problems were identified as a root cause in 72 percent of 47 cases (The Joint Commission, 2004). Research on inter-professional collaboration remains complicated due to the variation in study settings, varied definitions and measures of collaboration, and types of interventions (D'Amour, Ferrada-Videla, San Martin Rodriguez, & Beaulieu, 2005). This leads to difficulty with the generalization or replication of studies. It remains unclear how an inter-professional collaborative practice environment, guided by the CCM framework, influences health outcomes for patients with chronic disease.

APN-physician collaborative practice. The literature sources specifically examining nurse-physician collaborative practice were primarily descriptive in nature, outlining the roles of nurses functioning in a collaborative practice environment. In a two-group, quasi-experimental study of

1,207 medical inpatients, NP-physician collaboration for care (n=581) was compared to usual management (n=626) (Cowan et al., 2006). The NP interventions included (a) case management, (b) facilitation of communication and collaboration among the physicians and nurses, (c) leading and actively implementing timely processes after the daily multidisciplinary rounds, (d) adjusting antibiotic regimens to the narrowest spectrum based on culture reports, (e) enforcement of disease specific clinical pathways, and (f) expediting discharge planning. In addition, the NPs continued patient contact up to 30 days post discharge through follow-up telephone calls twice in the first week and once per week thereafter. At follow-up, the NP assessed the patient's medication adherence, adverse drug reactions, symptom management, and functional status. The NP contacted the primary care physicians if changes in patient management were required.

The findings of Cowan et al.'s (2006) study included a significantly reduced length of stay in the intervention group (5 +/- 6.3 versus 6.01 +/- 6.9 days, p=0.0001) equivalent to a cost savings of US$1,707 per day for one day of earlier discharge. There were no statistically significant differences between the groups in the readmission rates or mortality within the first four months after discharge. The researchers concluded that NP-physician collaboration results in a cost savings while not compromising readmission and mortality rates for this group of medical inpatients. Again, a component of this health care approach was the development of a standardized practice protocol clearly defining the NP scope of practice for the intervention group.

In summary, there is a paucity of research examining the APN-physician collaborative practice environment. Despite the inference that an inter-professional collaborative practice environment improves patient outcomes, the key element of the collaborative environment associated with this improvement is unclear. The studies lack a theoretical model to guide the intervention design or support a clear definition of collaboration. Further research is required to determine how a collaborative practice environment between the APN and physician influences patient outcomes

for chronic disease management. The following section reviews the research broadly examining chronic disease self-management, with specific reference to interventions focused on the use of case management, shared decision-making, collaborative patient care, and adherence enhancing interventions.

Patient disease self-management. At the centre of the CCM is patient disease self-management, which encompasses the decisions and behaviours that patients with chronic illness make from day-to-day. Supporting patient's development of disease self-management capacity includes interventions or processes focused on teaching individuals to manage their illness through an improvement in the knowledge and skills needed to perform daily self-care, manage crisis, make lifestyle changes, and informed decisions (Bodenheimer et al., 2002). Effective self-management support means more than just telling patients what to do. It means the patient participates in the self-management plan, thereby acknowledging a central role in maintaining their health. A basic premise of self-management is that people want to live long and healthy lives, even if they do not always do what is best for them or make the changes recommended by their healthcare providers. The evidence in support of disease self-management is strong, however not all interventions to teach patient disease self-management skills are effective (Tsai et al., 2005).

A meta-analysis of 53 RCTs, examining chronic disease self-management interventions for older adults with hypertension, osteoarthritis or diabetes, found a statistically and clinically significant pooled ES of -0.36 (95% CI, -0.52 to -0.21) for decreased HbA1c, a 5 mmHg decrease in systolic blood pressure (ES, -0.39 [CI, -0.51 to -0.28]), and 4.3 mmHg decrease in diastolic blood pressure (ES, -0.51 [CI, -0.73 to -0.30]). In addition, the pooled effects of self-management interventions were significant for reduction of pain and improved functional outcomes in patients with osteoarthritis. The authors could not identify the specific elements of the self-management programs that predicted successful outcomes (Chodosh et al., 2005).

In a Cochrane systematic review examining 16 trials of disease management services for patients with heart failure, interventions were classified into three categories, (1) multidisciplinary (e.g., holistic approach to care, bridging the gap between hospital admission and discharge, delivered by a team) (n=3), (2) case management (e.g., intense monitoring of patients following discharge in specialty clinic, telephone follow up, home visits) (n=11), and (3) clinic interventions (e.g., inpatient, outpatient or community based interventions or packages of care) (n=2) (Taylor et al., 2009). Specialist nurses were common to all studies, with the majority of interventions actively promoting an improvement in patient disease self-management.

Case management. The Case Management Society of America defines case management as a "collaborative process which assesses, plans, implements, coordinates, monitors, and evaluates options and services to meet an individual's health needs through communication and available resources to promote quality cost-effective outcomes" (Taylor, 1999, p.2). Case management originated in the social work disciplines, with its first documented use in mental health and more recently implementation in acute care settings (Zwarenstein, Reeves, Straus, Pinfold, & Goldman, 2009). Within the CCM, case management represents a process, which supports disease self-management through the development of a collaborative care relationship and the maintenance of a continuity of care, between the patient and healthcare professional.

In the Cochrane review discussed above (Taylor et al., 2009), results of the case management studies, considered of moderate quality, showed a statistically significant improvement in survival for the intervention group, odds ratio 0.68 (95% CI, 0.46 to 0.98, p = 0.04). There was no difference in mortality rates between the groups. In seven of the case management studies, researchers suggested that case management may be associated with a reduction in heart failure readmissions during follow-up, odds ratio 0.52 (95% CI, 0.39 to 0.70). One study, of a multidisciplinary intervention, showed significantly reduced numbers of heart-failure related re-

admissions in the short term. Overall, the authors concluded that there was insufficient evidence to support clinic interventions to improve patient disease self-management, with the stronger evidence in support of case management interventions in terms of survival and associated reduction in hospital re-admissions (Taylor et al., 2009).

The driving force behind case management is the need for a holistic health and wellness philosophy along a continuum of care, which arose from the loss of a continuum within the episodic and acute care focus of hospital-based tertiary models. Inherent in case-management is care coordination and the development of a quality relationship between the patient and healthcare professional that persists across time (Bower, 1992). The concept of a care-continuum is a key element within case management where a single healthcare professional oversees, manages, coordinates, and advocates for the health care of a given group of patients over time. The coordination of care includes supporting patient navigation through multiple services, diagnostic, and treatment regimens in a way that avoids complications, delays, and duplications.

Collaborative care. It is important to distinguish between 'collaborative practice' and 'collaborative care'. Collaborative care is the interaction and relationship between the healthcare professional and the patient, which guides and supports patient disease self-management (Wagner, 1998). Collaborative practice refers to the relationship between healthcare professionals. All interventions associated with patient disease self-management in the CCM include collaborative patient care because of the patient-centred focus of the approach. The development of a collaborative relationship between patients and healthcare professionals strengthens and supports self-care in chronic illness while assuring that effective medical, preventive, and health maintenance interventions take place (Von Korff et al., 1997). Healthcare professionals using collaborative, patient-focused care acknowledge that patients have as much expertise in their care

as their provider, which sets this approach apart from other models of health care (Bodenheimer et al., 2002).

The majority of research on collaborative patient care has been carried out in primary care mental health settings (Fletcher, Bower, Gilbody, Lovell, Richards, & Gask, 2009). In particular, these studies examined interventions as exemplars of collaborative care, which included proactive patient screening, education, and case management. Studies based on strengthening collaboration between the patient and healthcare professional, there-by strengthening the relationship, have demonstrated positive outcomes including greater patient satisfaction, adherence to treatment plans, higher self-reported health status, better emotional health, and improved symptom relief (Lewandowski, 1995; Tsai et al., 2005; WHO, 2002). Collaboration with the patient encompasses aspects of chronic illness self-management such as choices, control, and consequences (Rubin, Anderson, & Funnell, 2002) in addition to elements of shared decision-making, problem solving, and mutual goal setting (Neale, 1999).

Shared decision-making. Shared decision-making, as an element of collaborative care and patient disease self-management, assumes patient participation in health care decisions (Makoul, 2005). The aim in the care of kidney transplant patients is to (a) support patients' understanding of the treatment and evidence underpinning guidelines post transplant, including the risks and benefits associated with various treatment options; b) help patients clarify their values associated with the outcomes of choices, and c) reach informed, higher quality decisions based on patients' values. When patients have personal uncertainty related to a health care management decision, healthcare professionals should determine the source of this uncertainty. Common modifiable sources of patient uncertainty include inadequate knowledge of options, unclear understanding of the values associated with the option or outcome, and individuals feeling unsupported during the process of decision-making (O'Connor et al., 2007). The CCM has not traditionally included

shared decision-making as one of the key elements, however patient involvement in health decisions is a key factor related to improving satisfaction with care (O'Connor et al., 2007).

For the purposes of this study, supporting patient decision-making is included as an important element associated with collaborative patient care and incorporated into the structure of chronic disease self-management. The RNAO (Bruner et al., 2009) recently published a best practice guideline on decision support for adults living with CKD. The purpose of the guideline was to help nurses recognize when patients experience decisional conflict and to support their involvement in making quality decisions. Among the recommendations was the need for nurses to be aware of decisions required of patients with CKD, to screen for and identify the source of patients' decisional conflict, and understand the difference between providing patient education and decision support. The development of a collaborative relationship between the healthcare professional and patient may enhance decision support through the continuity of this relationship and the ability to monitor the patient's decisional needs over the trajectory of their disease.

In summary, despite advances in technology and treatment standards for CKD, end-stage renal disease and transplantation, many people are still not achieving optimal outcomes, resulting in devastating complications that lead to a decreased quality of life, increased morbidity, and mortality (de Mattos et al., 2005; Gill et al., 2003; Go et al., 2004). As mentioned previously, these suboptimal outcomes are, in part, the result of an approach to healthcare in which chronic disease management is not the standard practice. Typical approaches to kidney transplant care often assumes the healthcare professional's role is to tell the patient what to do and the patient's role is to comply with the recommendations. Healthcare professionals generally measure disease management success as the patient's ability to adhere to a predetermined care approach that may be suited to fit the patient's disease, yet not designed to fit the patient's priorities, goals, resources, culture, and lifestyle (Bodenheimer et al., 2002).

The goal of chronic disease self-management is to enable the patient to become a knowledgeable and active participant in his or her care by understanding the nature of the illness and its treatment, identifying emerging health problems and reversible stages early, adjusting and adhering to self-care behaviours, and making needed changes in health habits (Wagner, 2000). The development and promotion of behaviour change in patients with chronic disease is a key process within disease self-management. In APN led approaches to health care, for patients with chronic disease, pro-active screening for medication adherence is an integral part of supporting patient disease self-management (Sherry, Simmons, Wung, Johnson, & Zerwic, 2003).

Adherence enhancing interventions. Adherence, most commonly defined as "the extent to which a person's behaviour, taking medications, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider" (Sabaté, p3, 2003), continues to be used inter-changeably with the term compliance (Bissonnette, 2008). Adherent behaviour purportedly suggests that a patient agrees with the prescribed recommendations rather than just passively accepting and following the recommendations (Evangelista & Dracup, 2000; Sabaté, 2003). Some authors describe the main function of such terms as compliance and adherence as ideological in that these terms serve as a framework through which healthcare professionals convey their ideas concerning how patients should behave (Bissell et al, 2004; Britten, 2001; Donovan & Blake, 1992; Hearnshaw & Lindenmeyer, 2005; Trostle, 1988). The newest term concordance is an attempt to describe adherence or compliance less paternalistically by suggesting that patients and health professionals come to a mutually agreed upon regimen through a process of collaborative care involving negotiation and shared decision-making (Bissell et al., 2004; Bissonnette, 2008; Gray et al., 2002; Jones, 2003; Stevenson Cox , Britten, & Dundar, 2004).

Medication non-adherent behaviour is any patient initiated omission or adjustment of a medication dose or frequency not prescribed by or discussed with the healthcare professional, regardless of the underlying rationale (Chapman, 2004). Measures of patient medication adherence, used in research, include patient self-report questionnaires, pill counts, electronic monitoring devices, prescription record reviews, direct measurement of the drug metabolites in blood or urine, and outcome measures associated with a reduction of the specific disease related symptoms (Farmer, 1999; Krousel-Wood, Munter, Jannu, Desalvo, & Re, 2005). Within the adherence literature, the use of patient self-report questionnaires receives frequent criticism because of the dependency on patient honesty and the tendency for overestimation of medication adherence by patients (Chapman, 2004). Chapman (2004) asserts that, although there are a number of questionnaires that identify a patient's risk for non-adherence, the most accurate measure is the patient's admission to an alteration of prescribed medications. Chapman (2004) suggests that direct patient questioning, by the healthcare professional, to identify instances of patients altering their prescribed medications, may be a more practical approach for clinicians in the practice setting, than measures such as patient self-report questionnaires or electronic monitoring devices.

The majority of adherence enhancing interventions are categorized as behavioural change strategies (Haynes et al., 2005). The behaviour change techniques commonly used include behavioural contracting, behavioural cues, and patient self-monitoring. No single category or adherence enhancing intervention has been found to be more effective than any other (Christensen, 2004). The largest and broadest meta-analysis of interventions to improve patient adherence with medical regimens included 153 studies (116 RCTs and 37 non-random comparisons) published between 1977 and 1994 (Roter, Hall, Merisca, Nordstrom, Cretin, & Svarstad, 1998). The authors classified the interventions as educational (i.e., verbal or written with a knowledge based emphasis

designed to convey information), behavioural (i.e., targeting specific behavioural patterns through skill building, practice, modeling, contracting, tailoring or rewards), and affective strategies (i.e., appealing to feelings, emotions, social relationships through counselling techniques). The adherence indicators included (a) health outcomes (e.g., blood pressure and hospitalization), (b) direct indicators (e.g., drug metabolites in urine or blood), (c) indirect indicators (e.g., pill counts or refill records), (d) subjective reports (e.g., patient self-report), and (d) utilization (e.g., appointment keeping). The diagnostic categories included primary prevention (n=31), hypertension (n=24), mental health (n=13), and diabetes (n=12).

There were significant positive effects for all the adherence indicators (combined Z values >5 and< 32, $Z>4.0$, $p<0.0001$) in the intervention group as compared to non-intervention control groups in studies of interventions used to improve adherence. The largest positive effects (unweighted) were evident for the adherence indicators as measured by prescription refill records (ES=.60), pill counts (ES=.27), and drug metabolite measurement in blood or urine (ES=.30). Although smaller in magnitude, positive effects were evident through the adherence indicators of improved health outcomes (e.g., blood pressure, hospitalizations) (overall ES=.19) and utilization (e.g., appointment keeping, appointment making, preventative visits) (overall ES=.23). The authors concluded that no single strategy showed any clear advantage compared with another, whereas comprehensive interventions combining cognitive, behavioural, and affective components were more effective than single-focus interventions (Roter et al., 1998).

Broadened adherence intervention strategies, the outcomes in specific disease categories, and specific interventions to enhance medication adherence alone were examined in a more recent Cochrane systematic review (Bosch-Capblanch, Abba, Prictor, & Garner, 2009). The first review included 30 trials, to assess the effects of contracts between patients and healthcare practitioners on patients' adherence to treatment, prevention, and health promotion activities. The authors

concluded there was limited evidence that contracts contribute to improved adherence (Bosch-Capblanch et al., 2009). A second Cochrane review examined 21 studies of the effectiveness of interventions for improving adherence to treatment recommendations in people with type-two diabetes (Vermeire, Wens, Van Royen, Biot, Hearnshaw, & Lindenmeyer, 2009). The interventions examined included nurse led strategies (n=3), home aids (n=2), diabetes education (n=4), pharmacy led (n=5), dosing and frequency adjustments (n=3), and solitary intervention categories (n=4).

Vermeire et al. (2009) in the second Cochrane review, reported on three nurse led interventions. The first study (n=28, RCT) compared the effectiveness of education classes, including weekly nurse telemedicine 'home visit' to usual care over three months. There was a statistically significant reduction in mean HbA1c level by 0.4%. There were no significant changes in quality of life measures. In the second nurse led study (n=262, RCT) a 12-month telephone nurse-led follow-up intervention in which a nurse telephoned patients weekly to talk about self-care, medication adherence, and symptoms was examined. There was a small but statistically significant ($p = 0.04$) lowering of HbA1c moreover, patients in the intervention group reported fewer (-10%) diabetes related symptoms as compared to the control group.

In the third nurse led intervention study (n=748, controlled before/after study), a 12-month telephone follow-up program focused on (a) improving participants' understanding of their disease, with emphasis on the importance of adhering to standards of care, and (b) providing support to assist patients in their behaviour and lifestyle change. The authors assessed the patients' subjective reports of adherence and measured utilisation of medical services. There were no significant differences in the mean scores for medication adherence, completing recommended medical tests or in the use of preventive health services. In the remaining studies, Vermeire et al. (2009) noted, despite some positive study results, the studies had numerous methodological flaws,

which included (a) poor or absent definition of adherence, (b) low number of participants, (c) lack of a power calculation, and (d) the assumption that HbA1c levels directly reflect adherence. The authors of this Cochrane review concluded that the evidence has yet to demonstrate whether any adherence enhancing interventions in type-two diabetes, are truly effective.

The next Cochrane systematic review (Haynes, Ackloo, Sahota, MacDonald, & Yao, 2008) presented here, which updated the prior 2005 review of 57 studies (Haynes et al., 2005) with 24 new studies, examined the effectiveness of interventions for improving medication adherence. A number of chronic disease states were included in this updated review; the majority of the included studies examined adherence in human immunodeficiency virus (n=12) and hypertension (n=12). The review did not include any studies involving patients with CKD, ESRD or kidney transplantation. In the review, the authors identified 21 broad intervention strategies including; patient instruction, patient counselling, computer assisted monitoring or counselling, manual telephone follow-up, family intervention, regimen simplification, self-monitoring, and reminder systems. Each broad intervention category included a number of other less frequently used strategies, resulting in 93 variations of adherence enhancing interventions.

When compared to usual care, 41 of the 93 interventions examined in the 81 studies (combined 57 + 24 new studies) were associated with statistically significant increases in medication adherence. In addition, 29 interventions resulted in statistically significant improvement in the treatment outcomes. Of the 24 new studies added to this updated review, five showed positive effects of interventions on adherence and outcomes. Three of these studies involved health professionals other than physicians, such as a nurses or pharmacists, leading the intervention. The authors suggested that the effectiveness of adherence interventions led by non-physician health professionals requires further investigation, as these practices may be more reflective of what is feasible in the actual health care settings.

In summary, the evidence for the influence of adherence enhancing interventions on patient outcomes is promising although there remains limited reporting on their effects in CKD or transplantation. All of the Cochrane systematic reviews make similar conclusions, regardless of disease, intervention category or outcome measurement. The authors consistently comment on the lack of rigour noted within the study designs, unclear definition for adherence, the inability to assess effects of interventions or components separately, small sample sizes, and relatively short term follow-up (e.g., 24 months). On a more positive note, authors suggest that for long-term treatments, simplifying dosage regimen, and combinations of thorough patient education, counselling, follow-up and patient self-monitoring may improve adherence and treatment outcomes (Haynes et al., 2008).

Healthcare professional decision support/clinical information systems. In the chronic care model, decision support is defined as the existence and accessibility of evidence-based standards of care to guide healthcare professionals' clinical decision-making (Wagner et al., 2001). It is crucial to promote kidney transplant CKD clinical care that is consistent with scientific evidence and patient preferences. Treatment decisions need to be based on explicit, evidence-informed guidelines supported by clinical research, such as the KDIGO (2009) and NKF K/DOQI guidelines (NKF, 2002; 2003; 2003a; 2004; 2004a; 2006) in order to enhance the delivery of quality care. Healthcare professionals should also discuss these evidence-based treatment recommendations with patients, so they can understand the principles behind their care and make informed decisions.

Health care delivered to kidney transplant CKD patients falls short of optimal evidence based care (Akbari et al., 2007; Gill et al., 2002). A U.S. audit assessing 439 quality indicators found that adults receive only half of the guideline recommended care (McGlynn et al., 2003). The most common single intervention used and evaluated to optimize the implementation of evidence-based guidelines is reminders (Grimshaw et al., 2004). In a systematic review of the effectiveness of

guideline dissemination and implementation strategies, reminders made up 13% (n=38) of the 309 single interventions (Grimshaw et al., 2004). The studies included in this systematic review included a wide range of targeted behaviours (e.g., prevention services, general management, prescribing, discharge planning, financial, and procedures) and settings (e.g., ambulatory care, primary care, inpatient, specialist outpatient, and military medical centre). A reminder is defined as "patient or encounter-specific information, provided verbally, on paper or on a computer screen, which is designed or intended to prompt a health professional to recall information." (Grimshaw et al., 2004, p 8). The results of this systematic review suggest that reminders are a potentially effective approach for increasing guideline implementation, and are more likely to result in moderate improvements in the process of care.

Paper-based reminders have existed for many years, and range from notes on a patient's chart to standardized pre-printed physicians orders. More recently, with the advances in point-of-care technology, computer-based reminders have been implemented in an attempt to narrow the gap between care that is recommended according to the latest research, and what is done in the practice setting (Shojania, Jennings, Mayhew, Ramsay, Eccles, & Grimshaw, 2010). A systematic review by Shojania and colleagues (2010) included 28 controlled trials evaluating the effects of various computer-based reminder systems. This review, consisting of reminders to prescribe certain medications, vaccinations or diagnostic tests, showed small to moderate benefits. Physician practice improved by a median of 4% and in eight of the studies the patient's health outcomes improved by a median of 3% (Shojania et al., 2010). These results are limited by the heterogeneity of the interventions and the lack of detailed descriptions of the interventions.

A similar systematic review included 70 RCTs that compared a decision support system to no system or an alternate system (Kawamoto, Houlihan, Balas, & Lobach, 2005). The reviewers defined a clinical decision support system as "any electronic or non-electronic system designed to

aid directly in clinical decision making, in which characteristics of individual patients are used to generate patient-specific assessments or recommendations that are then presented to clinicians for consideration." (Kawamoto et al., 2005, p 2). The objective of this review was to identify the features of clinical decision support systems associated with improvements in clinical practice. Four features were found to be independent predictors of improved clinical practice: (a) support provided automatically as part of clinician workflow ($p<0.00001$), (b) support delivered during the time of decision-making ($p=0.02$), (c) provision of specific recommendations ($p=0.03$), and (d) computer used to generate the decision support ($p=0.03$) (Kawamoto et al., 2005). The authors suggest that these features reflect an ease of access for clinicians and therefore an effective clinical decision support system must be readily accessible and require minimal clinician effort.

In summary, effective chronic care is virtually impossible without information systems that assure ready access to key data on individual patients as well as populations of patients (Wagner, Davis, Schaefer, Von Korff, & Austin, 2002). Clinical information systems can enhance the care of individual patients by providing timely reminders about needed services and summarize data to better track and plan care. At the population level, clinical information systems may assist in the identification of groups of patients needing additional care as well as facilitate performance monitoring and quality improvement efforts (Wagner et al., 2002). In the absence of specialist or specialty group expertise, computer decision support systems may meet some of the day-to-day needs for expert advice.

Simple, integrated, computer-based clinical reminder systems for healthcare professionals are consistently effective in promoting recommended preventive procedures and behaviours in patients (Bodeinheimer et al., 2002; Toth-Pal, Nilsson, & Furhoff, 2004; Shojania et al., 2010). A meta-analysis of computer reminders for healthcare professionals showed improved preventive practices, compared with the control practices, for vaccinations, breast cancer screening, colorectal

screening, and cardiovascular risk reduction (Toth-Pal et al., 2004). While reminders for CKD and ESRD were not included in this meta-analysis, many of the aspects of the cardiovascular risk reduction reminders include services that should be provided for people with CKD, ESRD and transplant, such as blood pressure checks, hypertension follow-up, dietary assessment, counselling, and cholesterol screening.

Overall Summary

The CCM, developed by Wagner (1998) and based on direct clinical experience, integrates elements believed to foster improvements in outcomes for people with chronic health conditions. Use of the model, as a guide to practice in patients with transplant CKD, promotes the interaction of informed and motivated patients with proactive healthcare teams focused on supporting patient self-management skills to maintain their overall health and kidney function throughout the trajectory of their disease (Wagner, 2000). Layering structure and process measures onto the CCM broadens the evaluation to include components reflective of recommended clinical practice guidelines and standards for the management of CKD in kidney transplant patients. The World Health Organization (2002) attributes up to 50 percent of the mortality from the ten leading causes of death to lifestyle behaviours that cause or complicate chronic illness. Finding strategies for preventing and managing chronic conditions will pose a major challenge for health care in the 21st century. Effective, well-tested and re-structured care based on the CCM, which refocus health provision in such a way that care is evidence-based and patient-centered, allows for enhanced patient disease self-management support and secondary prevention (Glasgow, Orleans, & Wagner, 2001).

The CKD patient population includes kidney transplant patients with chronic disease in the form of chronic kidney or graft dysfunction. To optimize clinical outcomes, the kidney transplant CKD patient requires ongoing treatment monitoring, and disease self-management support. Co-

morbidities such as diabetes, cardiovascular disease, and hypertension, in addition to the number of medications a patient takes, increases the burden and challenge patients face daily while trying to manage their disease. Compounding the variation in clinical target achievement for kidney transplant patients are the adverse effects of lifelong immunosuppressant therapy. A patient's medication taking behaviour and adherence to immunosuppressant's have a direct influence on his/her kidney graft function, with any variation in the prescribed therapy increasing the risk for acute and chronic graft failure (Butler et al., 2004). A patient's decision to stop or alter his or her immunosuppressant post transplantation is associated with up to 36% of chronic kidney graft failures (Butler et al., 2004; Didlake et al., 1988; Nevins & Matas, 2004).

Challenges faced by healthcare practitioners in effectively managing patients with chronic disease have led to recommendations for the development and evaluation of chronic disease management strategies that incorporate effective patient communication, education, promote adherence, and encourage disease self-management in a cost efficient manner (Sabaté, 2003). Suggested approaches to chronic disease management include case management in a collaborative inter-professional environment with APNs, chronic disease patient self-management strategies and goals, clinical practice guidelines, and patient feedback (Sabaté, 2003). The development and implementation of an APN led inter-professional collaborative chronic care approach for kidney transplant CKD patients is a feasible and alternate approach to enhance outcomes in a medically complex, high-risk patient population.

Chapter Three

Methods

Aims

The purpose of this study was to examine and evaluate the effectiveness of an APN led inter-professional collaborative chronic care approach on achievement of clinical outcomes and care processes for patients with kidney transplant CKD.

Design

The study design was a non-randomized, controlled trial using propensity-score matching to account for potential confounding variables and selection biases in a non-randomized sample. The propensity-score, matched-pairs design is an alternative method applicable when random assignment is not possible or practical, as in retrospective or observational studies (Shadish, Cook, & Campbell, 2002). Randomization was not possible in this study as the control group was only accessible retrospectively through the use of a pre-existing clinical database. The intervention group and retrospective control patients were propensity-score matched based on the co-variates of eGFR, age, sex, kidney donor type and diabetes. For comparative purposes, alternate propensity-score models included the variables of eGFR, age and sex, or eGFR alone.

Setting

The setting was one ambulatory care, kidney transplant clinic at a large academic health science centre, serving a population of 1.1 million. The transplant clinic provides post-kidney transplant/nephrology related health monitoring and medical follow-up by an inter-professional team that includes four rotating transplant nephrologists, a full-time renal pharmacist, renal dietitian, social worker, and APN, in addition to two full-time and three part-time RNs. The patients had their kidney transplant at the same health care facility or transferred from another program, if they moved to this region. The transplant clinic activity for September and October of

2008 ranged from 70 to 118 patients per week, with an average of 91 per week. The range of daily clinic visits was 9 to 29, with an average of 19 per day. The transplant healthcare team followed 656 post-transplant patients. Implementation of a new APN role for the kidney transplant program occurred in February of 2005. The implementation of the APN role resulted in the establishment of a kidney transplant clinic for patients with CKD. The APN in the role was the researcher for the TARGET study.

Sample

The target population for this study was adult kidney transplant CKD patients, over the age of 18, followed at the kidney transplant clinic from January 2003 to December 2009. The intervention group included all eligible patients transferred into the APN collaborative chronic kidney care, transplant clinic as of January 2006. The control sample consisted of a retrospective group of eligible kidney transplant CKD patients in the kidney transplant care clinic in 2003, followed under the traditional nephrologist led healthcare approach.

Inclusion criteria.

1. One or more years since kidney transplantation.
2. A CKD classification of stage three or higher, defined as eGFR $\leq$ 60 mL/min/1.73 m² for three months or greater, as measured by the abbreviated Modification of Diet in Renal Disease (MDRD) equation.

Exclusion criteria.

1. A clinical diagnosis of acute kidney graft rejection.
2. Active treatment for malignancy.

Data Collection Procedures

Research assistants collected the data from both groups at baseline and at 12 months post intervention. The assistants completed chart audits and extracted data from existing clinical

information systems for the intervention group (see table 3.1). The researcher identified the retrospective control group from an Excel database, which clinicians developed in 2003 to determine the prevalence and clinical characteristics of kidney transplant CKD patients followed at the transplant clinic at that time under the traditional transplant care approach. The charts were not accessible for this group of renal transplant CKD patients therefore, no data was available for specific audit of medication non-adherence events or the number and content of patient and health care provider interactions. Research assistants with the Kidney Research Centre, experienced and familiar with chart audits and data collection procedures, performed all data extraction and data entry into a password protected Excel data worksheet developed for the study.

Table 3.1

Data Collection Procedures and Study Timelines (2003 to 2009)

Timing	**Measures**	**Intervention group**	**Control group**
Baseline	Demographic/characteristics	N=61	N=119
	Propensity-score matching	n=40	n=40
12 months post intervention	Process Measures • Implementation of standards of care	n=40	n=40
	Outcome data • Clinical target score • Hospitalizations • Emergency visits	n=40	n=40
	• Intervention user rate (dose) • Medication adherence (yes/no)	n=40	

The research assistants first entered the data onto a case report form (see Appendix II), and then transferred this information to the Excel database. For verification purposes, the research assistants retained copies of all source documents and placed these in binders along with the original case report form for each patient. All documents and binders were stored in a locked cabinet in the principal investigator's office. The principal investigator carried out cross-

verification of the case report forms, with the source documents and the Excel database, for the first 20 cases and every fifth case thereafter. The verification of the first 20 case report forms identified errors on 9 of the forms, which consisted of missing data elements (n=67), target outcome incorrectly marked (i.e., target ranges on case report form for reference comparison, see appendix II) (n= 2), and medications incorrectly noted as not receiving (n=9). The additional 7 case report forms, or every fifth case, had only 3 errors on 1 form, in which 3 data elements were left blank. Errors in the data abstraction and entry were reviewed with the research assistants on a weekly basis. The research assistants remained blinded to the rationale and outcomes of the study, and did not read the research proposal. The study proposal received approval from the research ethics review board (Appendix III).

Intervention

Intervention group. In 2006, kidney transplant patients with CKD began receiving care within an APN led collaborative inter-professional practice clinic environment. The transplant CKD clinic setting consisted of four clinic rooms with patients scheduled at 20-minute intervals, using all rooms concurrently. The scheduling interval allowed for a 40-minute clinic appointment, with seven patients scheduled one morning from 08h00 to 11h30 per week. The transplant nephrologist assigned to the clinic for that week was concurrently involved in a kidney transplant clinic and therefore was available for consultation with the APN as required. For kidney transplant CKD patients with an acute change in health or medical issue beyond the scope of the APN's practice, a collaborative review, as per medical directives, occurred between the APN, transplant nephrologist and patient at the time of the clinic visit. Four transplant nephrologists rotated through the clinic on a weekly basis. The APN recommended patient return appointments based on the stability of the patient's health and time since transplant with a minimum recommendation for patients to return every two to three months if stable. Strategies based on the chronic disease management

focus (Bodenheimer et al., 2002; 2002a; Wagner et al., 2001) and clinical practice guidelines for kidney transplant CKD (NKF 2003; 2003a; 2004; 2004a; 2006) guided the patient interventions, which included reinforcement of patient disease self-management, shared decision-making, adherence enhancing interventions, and community resource access (see Table 3.2).

Table 3.2

Chronic Kidney Disease Management Patient Focused Strategies

Strategies	Description
Disease Self-Management	1. Weight management. 2. Nutritional management: sodium, phosphate, protein intake. 3. Risk factor reduction: sun protection, mosquito avoidance/protection. 4. Recognition and management of uremic symptoms. 5. Signs and symptoms of hypo/hyperglycemia. 6. Patient self-monitoring.
Shared Decision Making	1. End stage renal disease (ESRD) options including re-transplantation. 2. Referral to ESRD options education: vascular access or home dialysis. 3. Medication adverse drug effects and alternatives. 4. Vaccination status and options. 5. Lifestyle choices: smoking status, alcohol intake, exercise level.
Adherence Enhancing Behaviour	1. Increased contact between patient and provider. 2. Repeated/explicit monitoring of adherence by patient and/or provider. 3. Encouraging positive patient expectations for adherence improvement. 4. Provision of positive recognition/reinforcement for successful adherence. 5. Increasing awareness adherence will be evaluated with direct questioning. 6. Soliciting an explicit (written or verbal) patient commitment to adhere to specific treatment recommendation. 7. Provider reinforcement reflecting adherence is an important outcome.
Community Resources Accessibility	1. Referral to weight management program. 2. Referral to smoking cessation program. 3. Referral to rehabilitation program. 4. Referral to diabetes education program. 5. Referral to psycho/social/family counselling. 6. Referral to financial support services.

The intervention also included (a) the use of evidence-based standards of care in the form of medical directives to guide and outline the scope of practice for the APN (appendix IV), (b) a policy outlining the expectations and roles of each member of the inter-professional team

(appendix V), (c) a collaborative practice environment supported by weekly inter-professional patient rounds and APN-physician case review on the day of the patient clinic visit, (d) healthcare professional and patient interactions based on the CCM and collaborative care approach, with specific strategies for CKD self-management, and (e) a structured approach to monitoring and follow-up of clinic patients, based on clinical practice guidelines for CKD and kidney transplant patient management (table 3.3) (NFK 2003a; 2004; 2004a; 2006).

Table 3.3

Intervention Clinic Assessment Standards and Appointment Schedules

Health professional assessment standards	**Appointment frequency (months)**					
Holistic health assessment: diagnosis/treatment/monitoring *Advanced Practice Nurse/Physician Collaboration*	**2**	**4**	**6**	**8**	**10**	**12**
• Cardiovascular event risk factors • Co-morbidities • Adverse medical/health events • Kidney graft function, weight, vital signs • Uremic symptoms assessment • Immunosuppressant medication monitoring/adjustments • End-stage renal disease options assessment and discussion. • Medication taking behaviour/adherence • Adverse drug effects • Lifestyle risk factors: smoking, alcohol/illicit drug use, activity level.	X	X	X	X	X	X
Dietitian: Nutritional assessment/weight management	X	X	X	X	X	X
Social Worker: Psycho/social/life events counselling	X	X	X	X	X	X
Pharmacist: Medication review/assessment • Medication reconciliation/review: drug allergies, interactions, intolerances, adverse drug reactions, poly-pharmacy. • Patient adherence decisions/medication taking behaviour/medication self-adjustments.	X	X	X	X	X	X
Standard Laboratory Tests *Serum*: complete blood count, creatinine, urea, potassium, sodium, chloride, carbon dioxide, calcium, phosphate, albumin, random glucose, immunosuppressant drug level *Urine*: random urine albumin to creatinine ratio, urinalysis	X	X	X	X	X	X
Serum: fasting blood glucose, fasting lipid profile, parathyroid hormone, iron saturation, ferritin, B12, folate, iron		X		X		X
Serum: liver enzymes, creatinine kinase, * hemoglobinA1c *Initial screen then diabetic patients **24 hour urine collection	*X		*X			**

Health professional assessment standards. The APN, as case manager, focused the assessment of, and interaction with, the patient on health factors related to kidney graft function, as well as those factors influencing overall health/well-being and chronic disease self-management. These factors included recent adverse health events, progression of renal dysfunction, uremic symptoms, co-morbidities, cardiovascular disease risk factors, lifestyle risk factors, medication adherence and decisions around ESRD options.

The APN or the pharmacist reviewed, with the patient, their current medication list focusing the medication review on the patient's recognition of medication, name, dose, reason for taking, adverse drug reactions and medication adherence behaviour. The pharmacist provided the patient with an updated medication list as required. The APN and pharmacist asked directed questions about medication taking behaviour and adherence such as: "On average in one week how many times would you miss taking your anti-rejection medications (naming specific medication)?", or "Are there certain times or situations in which you are more likely to miss taking your medications (naming specific medication)?". Additional questions if problematic medication-taking behaviour included (a) "What do you currently do to help you remember to take your medications?", and (b) "Do you believe the medications you take help to prevent worsening of your kidney function?". The APN and pharmacist reinforced, with the patient, that any un-prescribed change in the dose of immunosuppressant therapy could have a negative effect on their kidney function. The healthcare professional documented these discussions in the patient's health record.

At each visit, the dietitian assessed the patient's nutritional and weight management status. The dietitian reviewed, with the patient, any recommended dietary restrictions, provided suggestions for food alternatives, and counselled on weight management strategies when appropriate. The social worker also assessed the patient, reviewing and discussing any advanced care directives, financial or social support issues identified during the interaction. In addition, the social worker

assessed the patient's overall coping response to his or her CKD stage and inquired about any major life changes (e.g., death of a friend or family member, new or job loss, move, retirement, divorce/ marriage).

The care management activities, which occurred outside the patient clinic appointment, included the APN review of laboratory and diagnostic test results, and review of current treatment plan or prescriptions based on the assessment of these results as available. Changes in the current treatment plan were also reviewed with the transplant nephrologist as outlined in the medical directives or with any acute changes in the patient's health status. The renal dietitian and pharmacist reviewed laboratory results, and within their scopes of practice, discussed and made recommendations to the APN for dietary or medication adjustments based on these results. The APN was available to patients for telephone consultation during the weekdays 08h00 to 16h00, for questions or follow-up, as all patients received the APN's contact number.

The inter-professional patient care team held weekly patient rounds attended by all transplant nephrologists in addition to the transplant fellow or resident assigned to the transplant program for that semester. These rounds included a discussion of the regular transplant clinic patients and the transplant CKD clinic patients. The transplant fellows or residents were not involved in the kidney transplant CKD clinic.

Control group: traditional approach for transplant care. In 2002-2003, the traditional transplant nephrologist led care, was in place for the retrospective control group of patients with kidney transplant CKD. At the time, four transplant nephrologists rotated through the clinic on a weekly basis. Additional healthcare professionals, involved with patient care, included RN's and by consult on certain days, a part-time social worker, and renal dietitian. It is important to note that all the RNs had specialization in nephrology and the Canadian Nurses Association nephrology certification was required to qualify for a position in the transplant clinic. The setting consisted of

four clinic rooms with patients scheduled at 10-minute intervals, using all rooms concurrently. The scheduling interval allowed for a 20-minute clinic appointment, with 20 to 25 patients seen five mornings per week, from 08h00 to 11h30. Physicians recommended patient return appointments based on the stability of the patient's health and time since transplant with a minimum recommendation for patients to return every three months if stable.

At each clinic visit, the RN responsibilities included escorting the patient into the clinic room, obtaining the patient's vital signs and weight, reviewing and updating the medication list and assessing the patient for any changes in health status since the last clinic visit. The RN provided patient education during the clinic visits or when the RN judged it necessary in relation to the patient's inquiries and seasonal recommendations. The most commonly discussed topics were: a) the importance of sun protection, b) strategies for the prevention of infection, c) need for annual physical, d) dietary restrictions as required, e) annual influenza vaccination, d) erythropoietin subcutaneous injection teaching, e) reinforcement of regular laboratory testing, and f) attendance at clinic appointments as recommended by transplant nephrologist. The RNs did not use any formalized document or guide to patient education, although they did have over 15 years of experience in the care of kidney transplant patients.

The majority of kidney transplant specific education occurred immediately after the kidney transplant surgery and during the first three months post-transplant. A documented protocol or standard of practice for the RN patient health assessment and education was not available in the clinic at that time. The physicians referred the transplant CKD patients to a specialist RN outside the transplant clinic setting for education on end-stage renal disease options. This focused on a review of the choices for dialysis (i.e., home hemo-dialysis, peritoneal dialysis, in-centre dialysis).The RN wrote a narrative progress note in the patient's health record reflecting the

assessment, discussion and any key issues that the patient or RN identified for review by the transplant nephrologist. Table 3.4 provides a comparison of the intervention and control group clinic activities, describing the key similarities and differences in the approaches to care based on elements of chronic disease management.

Table 3.4

Comparison of Intervention and Control Group Approaches to Clinic Care

Intervention group	Control group
Delivery system design	
1. APN/physician collaborative practice. 2. Four rotating transplant nephrologists. 3. Inter-professional health team continuity. 4. Weekly healthcare team rounds.	1. Physician/RN practice team. 2. Four rotating transplant nephrologists 3. Rotating fellows/residents/RNs. 4. Inter-professional discipline by consult. 5. No formalized team rounds.
Patient disease self-management support	
1. APN - patient telephone follow-up. 2. APN case management. 3. APN initiated ESRD discussions. 4. Chronic disease management oriented care. 5. Formalized medication reconciliation. 6. Targeted patient education on disease self-management strategies.	1. RN - patient telephone follow-up. 2. RN team nursing approach. 3. Physician initiated ESRD discussions. 4. Problem/tertiary oriented care. 5. Patient education non-standardized.
Clinician decision support	
1. Evidence based protocols/directives.	1. Standardized protocols not in use.

The transplant nephrologists assessed the patient after the RN. Physicians based their clinical decision-making on K/DOQI standards and relevant kidney transplant guidelines or research evidence available as of 2003 (NKF 2002, 2003, 2003a). The medical assessment focused on the diagnosis and treatment of acute changes in kidney graft function, recurrent kidney disease, co-morbidities such as hypertension, hyperlipidemia, anemia, diabetes, infection, malignancy, metabolic control, in addition to the monitoring and adjustment of immunosuppressant medication levels as appropriate.

Patient care activities, occurring outside the clinic time, included physician review of laboratory and diagnostic test results, treatment recommendations and prescriptions based on the assessment of test results. The clinic RN processed these orders and called patients with any changes or scheduled additional tests as prescribed. The RN was also available from 09h00 to 16h00 for patient or patient related telephone calls. There were no formalized patient care rounds or team meetings to discuss and review patient status.

Primary and Secondary Outcome Measures

Primary outcome. The primary outcome of interest was the optimization of patient achievement of the K/DOQI based clinical targets and the patients' participation in ESRD options discussions with a healthcare professional. In both groups, the clinical values, used to determine whether the clinical target was met, were based on the median of three laboratory results and blood pressure readings closest to the 12-month study end date. The target range for blood pressure in the intervention group differed from that of the retrospective control group due to the 2004 update of guideline recommendations for optimal blood pressure in patients with CKD (e.g., systolic blood pressure 130 current versus 140 past) (NFK, 2004). The research assistants entered these values onto the case report form and selected yes or no if the patients' median value was within the expected target range.

In the intervention group, the research assistants conducted a chart audit of the patients' health record for the 12-month study period. If the healthcare professional documented that, a discussion occurred with the patient about ESRD options, at any time during the 12-month study, the assistants marked that target as met. The retrospective control group database included a yes or no data element on whether ESRD discussions took place between a healthcare professional and the patient. The number of targets that were met by each patient was then calculated (see table 3.5).

The primary outcome measure was the proportion of patients in each group meeting seven out of the nine targets, or a target score of 78%.

Table 3.5

Primary Outcome Targets and Target Score

K/DOQI Based Targeted Standards and Goals	
Target Standard	Target Goal Met (yes/no)
1. Systolic blood pressure	≤ 130 mmHg (≤140*)
2. Diastolic blood pressure	≤ 80 mmHg (≤ 90*)
3. Hemoglobin	105-120 g/L
4. Low density lipoprotein (LDL)	< 2.6 mmol/L
5. Parathyroid hormone level (PTH)	< 33.0 pmol/L
6. Calcium	2.23 – 2.58 mmol/L**
7. Phosphate	0.6 – 1.80 mmol/L
8. Carbon Dioxide	21-32 mmol/L
9. End-stage renal disease options discussed	▪ Return to dialysis, re-transplant, palliation, ▪ Dialysis access options
Target Score Achieved	**Goal 7 out 9 (78%)**

* Blood pressure targets for control group.
** Adjusted for serum albumin using standard correction factors 0.02 mmol/L for every 10 units of albumin lower than 40.

In order to estimate the potential impact and therefore sample size, the target score was based on Akbari et al.'s (2007) cross-sectional study of 72 CKD and 72 kidney transplant CKD patients, in which, the CKD patients in the inter-professional approach to care achieved, on average, seven out of nine K/DOQI targets. The transplant CKD patients, in the traditional post transplant nephrologist led approach, achieved an average of four targets. Therefore, based on these findings, the score of 78%, or seven out of nine targets, is a reasonable outcome for the intervention patients in the TARGET study.

Secondary outcomes. The secondary outcomes included the number of hospitalizations, emergency department visits, and process measures. In both groups, all cause hospitalizations and emergency department visits during the 12-month study period were extracted from the hospitals'

clinical information system, which records a patient's hospital admission or emergency department encounter for only this hospital.

Process measures. The process measures included the implementation of K/DOQI treatment or management recommendations for the co-morbidities associated with CKD, primarily cardiovascular disease, hypertension, anemia, hyperlipidemia and hyperparathyroidism. The research assistants extracted these elements by chart audit for the intervention group and entered yes or no if implemented. The same data elements were available in the database for the control group and entered as yes or no if implemented. In both groups, the process measures were:

(1) treated with ACE-I/ARB as first line anti-hypertensive medication for blood pressure control;

(2) receiving erythropoiesis-stimulating agent (ESA) for anemia;

(3) receiving statin therapy for hyperlipidemia;

(4) receiving aspirin as a cardio-protective agent;

(5) receiving phosphate binders for hyperphosphatemia;

(6) serum levels measured for screening of hyperlipidemia and hyperparathyroidism: low-density lipoprotein (LDL) and parathyroid hormone (PTH).

In the intervention group, additional process measures included medication non-adherence events, chronic disease self-management, patient decision support, and community resource referral documented for patients by the healthcare professional. For this study, medication non-adherence is defined as any patient reported and non-prescribed adjustment of medications. The medications included all immunosuppressants and additional prescribed medications (e.g., antihypertensive agents, statins, calcium supplements, iron supplements). These data elements were not available for the control group. The research assistant entered each documented interaction, representing the above process measures, onto the case report form (Appendix I). The case report form included the following script to guide the research assistant in identifying

documentation in the patient's chart reflective of chronic disease self-management patient/provider interactions (Bodenheimer, MacGregor, & Sharifi, 2005).

> *The intervention/interaction consists of a documented encounter in which counselling, education, advice, teaching or instruction is received by the patient from the healthcare provider in the form of a discussion and/or written material. In order to qualify, the notation must include* ***at least one*** *of the following characteristics:*
>
> *(1) Involvement of the patient in the management of the disease (i.e. something that the patient will do, is able to do due to instruction, not something the provider will do).*
>
> - *We talked about the importance of appropriate foods and diet*
> - *Can state what foods to avoid for low-salt diet*
> - *Advised to do daily weights*
> - *Encouraged to walk 5-6 days/week, agreed will exercise more*
> - *Patient is reluctant to or is resistant to doing recommended risk management*
>
> *(2) Written material about the disease, medication, risk factors, complications is given to or discussed with the patient.*
>
> *(3) A checklist completed by provider or patient that indicates what type of counselling was given to the patient, or addressed at the visit (implies a discussion took place).*

Measuring the dose of chronic kidney disease self-management intervention. The dose of chronic disease management intervention was measured based on the amount, frequency and duration of the intervention (Reed, Titler, Dochterman, Shever, Kanak, & Picone, 2007). The amount was the quantity of intervention provided by the healthcare professional at one point in time, which represents the single intervention's strength. In this study, one unit of APN or healthcare professional documented interaction with the patient, reflective of a chronic disease management focused intervention was one documented event during that patient visit. The frequency was the number of times the patient received the intervention as measured by the number of clinic visits over the 12-month study period. The duration is the entire length of time over which the patient was exposed to the intervention, measured as the length of time patients were followed in the APN collaborative transplant CKD clinic in months.

Multiplying the amount of the intervention by the frequency then produces the quantity of intervention received by the patient. Dividing the quantity by the duration then produces an average dose, which has been termed the 'intervention user rate' (Reed et al., 2007). In this study, the dose of chronic disease management for each patient is the intervention user rate. To determine the intervention user rate, the calculation included the quantity of interventions provided by each discipline. One unit was equivalent to a single dose of the chronic disease management intervention, with the final dose measure considered a unit (dose) per patient visit.

The following provides a fictitious example of the calculation for the intervention user rate or dose of chronic disease management (CDM) intervention.

1. Amount = quantity of intervention as measured by number of CDM documentations at one clinic visit = 6.
2. Frequency = the number of times the patient was exposed to the CDM approach as measured by the number of clinic visits for each patient over the study period = 7.
3. Duration = the entire length of time over which the patient was exposed to the CDM approach as measured by the length of time followed in the clinic in months or study period = 12.
4. Amount x frequency = quantity = 6 x 7 = 42.
5. Total quantity/duration = intervention user rate (dose) = 42/12=3.5.

The dose of CDM intervention based on the above formulae is 3.5 units per patient clinic visit.

Sample Size Justification and Formula

The sample size for studies comparing proportions in two equally sized groups was the basis for the final calculation using the following assumptions (Whitley & Ball, 2002).

1. What is the desired level of significance or α level?

   $\alpha = 0.05$., associated $Z_{critical\ (crit)} = 1.96$ (for two-sided test).

2. What level of power (1-β) is desired?

β = .20, power = .80, associated $\mathbf{Z}_{\text{power (pwr)}} = .842$.

3. How large should the difference between the proportion in one group, and the proportion in the second group be for the difference to have clinical importance?

Estimates of the magnitude of difference between the control and intervention groups in the proportions meeting the clinical target, and therefore the estimate of sample size requirements, were based on Akbari et al.'s (2007) research. The proportion of transplant CKD patients who achieved clinical targets followed in the traditional transplant care clinic ranged from 7% to 85%, with a median of 43%. The proportion of non-transplant CKD patients who achieved the clinical targets followed in a renal insufficiency or CKD clinic applying a protocol driven approach to care ranged from 8% to 79%, with a median of 76%. The minimum expected difference is then represented by the difference between these two proportions (.76 - .43).

- p_1 = the expected proportion of patients achieving the target score in the intervention group = .76
- p_2 = the expected proportion of patients achieving the target score in the control group = .43
- $\bar{p}$ = the mean proportion = .76 + .43 /2 = .60
- D = the minimum expected difference = $p_1 - p_2$ = .76 -.43 = .33

Sample size formula.

$$N = 2\,[Z_{crit}\sqrt{2\bar{p}(1-\bar{p})} + Z_{pwr}\sqrt{p_1(1-p_1) + p_2(1-p_2)}]^2 / D^2$$

$$= 2\,[1.96\sqrt{2(.60)(.40)} + .842\sqrt{.76(.24) + .43(.57)}]^2 / .11$$

$$= 2\,(1.96\sqrt{1.32}\sqrt{.43}]^2 / .1089 = 2(1.96 \times 1.15 \times .66)^2 / .109 = 4.43/.11 = 40$$

Therefore, to detect a difference of .33 or 33% between the groups in the proportion of patients achieving the target score with a two-sided alpha error of 0.05 and a power of .80 a total sample size of 40 or 20 per group is required.

Statistical Analysis

Baseline characteristics between the intervention and control groups were compared using the Student's t-test for continuous variables or the Chi square test for categorical variables. All reported p-values were 2-tailed. The analysis included descriptive statistics to determine the distribution, mean, and median for all baseline variables.

Propensity-score analysis. A propensity analysis was undertaken to account for potential confounding factors and selection biases because of the non-random allocation of the two groups. The propensity-score matching model assumes that individuals, with the same characteristics used for matching, have an equal probability of being in either the intervention or the control groups (Foster, 2003). The propensity model matches each intervention patient to a control patient based on a propensity-score value. This results in a balance of the measured variables and an unbiased estimate of the expected difference in response to two treatments (Austin, 2008). The propensity-score for an individual is defined as the conditional probability of being treated given the individual's co-variates (D'Agostino, 1998).

Propensity-scores for "treatment" were calculated using multivariate logistic regression based on a primary and two alternate models. In the primary model, propensity-scores were calculated using eGFR, and the variables age, sex, diabetes, and living versus deceased kidney donor. These variables are suspected to influence group assignment or affect various outcome measures (e.g., blood pressure, lipid profile, hemoglobin, parathyroid hormone, carbon dioxide, calcium, and phosphate levels). The chosen confounding variables potentially influence the development of CKD or chronic graft failure. These variables may influence selection for the transplant CKD

intervention group due to their influence on the progression of CKD. The two alternate propensity models included age, sex with eGFR and eGFR only, to determine if the use of fewer variables, and therefore simplifying the propensity-score model, would influence the distribution of baseline co-variates and outcomes.

The propensity-score was used to match patients in the intervention group to a control patient by a 'nearest-neighbour' or 'greedy matching' procedure, which selected pairs. Initially matched pairs were identical to five decimal places of probability (Parsons, 2001). If no match existed at five places, matching would occur at four, three, two, and one decimal places. If no match existed at one decimal place then the intervention patient was excluded from the study.

The abbreviated Modification of Diet in Renal Disease (MDRD) equation was used to calculate eGFR as it is considered more accurate for patients with renal disease and less biased as compared with other methods of estimating GFR (NKF, 2002; Levey, Greene, Kusek, & Beck, 2000). In addition, changes to the calculation of eGFR occurred in February of 2008 due to a change in the laboratory analysis system. The IDMS (isotope dilution mass spectrometry) method was implemented for the standardization of creatinine assays in serum creatinine analysis therefore the eGFR calculations for intervention patients, using a serum creatinine drawn from February 2008 onwards, included the adjustment for IDMS calibration.

Outcomes Analysis

All statistical analyses were conducted using the Statistical Analysis Software (SAS, version 9.1), with the support of a statistician from the Ottawa Hospital Research Institute, Methods Centre. The Chi square test was used to test for differences in the proportions of achieved versus not achieved outcomes between the groups (e.g., target score, discussions on options for ESRD, implementation of K/DOQI standards). The Chi square test was also used to test for the difference in proportion of patients reporting medication adherence or non-adherence and achievement of

clinical outcomes (e.g., target score, discussions on options for ESRD, K/DOQI targets). The incidence rate ratio (IRR) was used to test for the difference between the groups in hospital admissions and emergency department visits. The Student's t-test was used to test for the number of patients achieving the target score based on the intervention user rate (i.e., chronic disease management dose) (see table 3.6). The Student's t-test and Chi square tests were chosen based on the assumptions of the propensity-score analysis. The propensity-score matching assumes the observations are independent as opposed to paired, and as a result, the matching algorithm (propensity) results in two 'independent' groups (Austin, 2008). The primary outcome was compared across the three propensity matched models to determine whether the outcomes differed significantly according to the model variables.

Table 3.6

Statistical Analysis

Research question/ Hypotheses (H)	Dependent variable(DV)/ independent variable(IV)	Outcome measure	Statistical test
1. Is there an association between patients' exposure to the APN led inter-professional collaborative chronic care approach and achievement of clinical targets and end-stage renal disease options discussions?			
H1: Patients exposed to the intervention are more likely to achieve the target score than controls.	**DV**: Achieved vs not achieved (Y/N). **IV:** Exposure to the intervention.	The % of patients achieving a clinical target score of 78%.	Chi square test
H2: Patients exposed to the intervention are more likely to participate in ESRD discussions than controls.	**DV**: Achieved vs not achieved (Y/N). **IV**: Exposure to the intervention.	The % of patients participating in discussions on ESRD options with a healthcare provider.	Chi square test
2. Is there an association between patients' exposure to the APN led inter-professional collaborative chronic care approach and number of hospital or emergency department visits?			
H1: Patients in the intervention group have fewer hospital admissions and ER visits.	**DV:** The total # of ER/hospital admissions. **IV**: Exposure to the intervention.	The rate of hospital admissions and emergency visits.	Incidence rate ratio
3. Is there an association between patients' exposure to the APN led inter-professional CKCM and implementation of K/DOQI treatment standards?			
H1: Patients exposed to the intervention are more likely to have K/DOQI standards implemented.	**DV**: Achieved vs not achieved (Y/N). **IV**: Exposure to the intervention.	The % of patients with K/DOQI standards implemented.	Chi square test
4. Does matching the groups using the propensity-score method, control for the differences in co-variates?			
H1: The groups will be equivalent using the propensity-score method for matching on co-variates as compared to matching on GFR.	**DV**: Co-variate distribution. **IV**: Propensity-score model.	The baseline distribution between groups when matched for age, sex, GFR, diabetes, donor versus GFR.	Descriptive
H2: The outcome results using GFR will be different from the results based on the co-variates of GFR, age, sex, donor, and diabetes.	**DV**: The outcome results. **IV**: Propensity-score model.	The difference in outcomes based on propensity-score model.	Descriptive
5. Within the intervention group, is there an association between number of patient's reported non-adherence, as measured by non-prescribed medication self-adjustment documentations, and achievement of clinical targets?			
H1: Patients reporting medication non-adherence events achieve fewer clinical targets as compared to adherent patients.	**DV**: Achievement of targets (Y/N). **IV**: Patient reports of non-adherence.	The % of patients reporting medication non-adherence events achieving targets.	Chi square test
6. Within the intervention group, is there an association between the chronic disease management intervention dose and patient achievement of targets?			
H1: Patients achieving targets receive a higher mean dose of chronic disease management intervention (intervention user rate-IUR).	**DV**: Achievement of targets (Y/N). **IV**: Intervention dose (IUR).	The # of patients achieving clinical targets.	Student's t-test

Chapter Four

Results

Baseline Demographic and Clinical Characteristic Findings

Between March 2006 and September 2009, 61 kidney transplant CKD patients with an eGFR $\leq$ 30 mL/min/1.73 m² and mean time since transplant of 125 (SD +/- 98) months, entered the APN led inter-professional collaborative CKD clinic. These 61 patients were propensity-score matched to a retrospective control group of 119 patients. The control group was a prevalent group of kidney transplant CKD patients, with an eGFR $\leq$ 30 mL/min/1.73 m² and mean time since transplant of 101 (SD +/- 85) months, who received care within the transplant nephrologist led clinic in October of 2003.

Propensity-Score Matched Baseline Variable Distribution

The sample size decreased from 180 to 80, with 40 matched pairs in the primary propensity-score matched model. The primary matching model using eGFR, age, sex, diagnosis of diabetes and kidney donor type, resulted in no statistically significant differences between the groups for those co-variates (see table 4.0). In the matched analysis, patients had an average age of 51 and an average eGFR of 21 mL/min/1.73 m² which represents stage four (eGFR 15-29 mL/min/1.73 m²) of CKD as defined by NKF-K/DOQI (2002). The time since transplant was not significantly different between the groups (p=0.32) and no significant difference was found in the primary cause of end-stage renal disease.

Table 4.0

Baseline Co-variates of Propensity-Score Matched Groups (N=80)

	Unmatched			Propensity-Score Matched		
Baseline Co-variates	I (%) n=61	C (%) n=119	P-value	I(%) n=40	C (%) n=40	P-value
Age- years *	52 ± 14	51 ± 14	0.51	51 ± 15	50 ± 14	0.69
eGFR mL/min/1.73 m² *	20 ± 5.1	27 ± 6.4	0.0001	21 ± 5.1	21 ± 6.1	0.80
Male, % *	67	59	0.27	60	60	
Diagnosis of Diabetes *	12 (20)	21 (18)	0.74	9 (23)	10 (25)	0.79
Living Kidney Donor *	20 (33)	36 (31)	0.78	14 (35)	12 (30)	0.63
Time since transplant- months	125 ± 98	101 ± 85	0.09	130 ±95	109± 91	0.32
ESRD-Primary Cause						
Diabetes	12 (20)	21 (18)	0.74	9 (23)	10(25)	0.79
Polycystic kidney	6 (10)	14 (12)	0.70	4 (10)	4 (10)	
Glomerular nephritis	12 (20)	39 (33)	0.06	5 (13)	11(28)	0.09
Hypertension	5 (8)	2 (2)	0.05	3 (8)	0 (0)	0.27
Interstitial nephritis	2 (3)	2 (2)	0.67	2 (5)	1 (3)	0.64
Obstructive reflux	4 (7)	13 (11)	0.39	3 (8)	3 (8)	
Lupus	0 (0)	4 (3)	0.17	0 (0)	2 (5)	0.16
Drug induced	3 (5)	2 (2)	0.27	1 (3)	0 (0)	0.27
Vasculitis	0 (0)	3 (3)	0.17	0 (0)	0 (0)	
Congenital renal dysplasia	8 (13)	8 (7)	0.19	5 (13)	5 (13)	
Immunoglobulin A nephropathy	4 (7)	0 (0)	0.004	3 (8)	0 (0)	0.07
Pyelonephritis	1 (2)	2 (2)		1 (3)	0 (0)	0.27
Unknown	2 (3)	9 (8)	0.19	2 (5)	4 (10)	0.34
Other	2 (3)	0 (0)	0.17	2 (5)	0 (0)	0.16

* Co-variates included in propensity-score model, ESRD=End-stage renal disease
p-values-Student's t-test for continuous variables, reported as mean ± standard deviation;
Chi square test for categorical variables, p-values 2-tailed, significant ≤ 0.05.
eGFR = estimated Glomerular filtration rate calculated using the abbreviated MDRD study equation (Levey et al., 1996), I=Intervention, C=control.

Primary Outcome Results

Primary research question: hypothesis one and two. The primary outcomes of interest were the proportion of patients achieving the clinical target score of 78%, and the proportion of patients participating in discussions related to end-stage renal disease options (see Table 4.1). The target score, set at 7 out of 9 potential K/DOQI targets, makes up the total score of 78%.

There was a significant difference (p=0.0001) between the intervention and control groups in the proportion achieving seven out of nine targets (78%). In the control group, 4 (10%) patients achieved 78% of the targets as compared to 27 (68%) in the intervention group. A significantly greater proportion of patients in the intervention group (p=0.0001) participated in end-stage renal disease options discussions, 35 (88%) as compared to 5 (13%) in the control group.

Table 4.1

Comparison of Proportion Achieving Target Score and ESRD Discussions

Primary Outcomes	**Intervention** n=40(%)	**Control** n=40(%)	**P-value**
78% Target Score achieved	27(68)	4(10)	0.0001
Participated in ESRD options discussions	35(88)	5(13)	0.0001

p-values - Chi Square test , Bonferroni corrected $\alpha < 0.01$, ESRD=end-stage renal disease

Achievement of individual targets. A significantly greater proportion of the intervention group, 31 (78%) achieved the target for low-density lipoprotein ($\leq$ 2.5 mmol/L, p=0.006), as compared to 6 (18%) in the control group (see Table 4.2). For this target, the value for the LDL was missing in 10 cases in the control group, and therefore the Fischer exact test was used to determine the difference as is indicated when 'expected' cells have fewer than 5 individuals. A significantly (p=0.004) greater proportion of patients in the intervention group achieved the calcium target (2.23 – 2.58 mmol/L), 35 (88%) as compared to 19 (51%) in the control group. A significantly (p=0.006) greater proportion of intervention patients achieved the PTH target, 29 (74%) as compared to 6 (18%) in the control group. There was no significant difference between the proportions in each group achieving the targets for systolic and diastolic blood pressure, phosphate or hemoglobin levels. A greater proportion in the control group 37 (95%) achieved the target level for carbon dioxide (21-32 mmol/L, p=0.02) as compared to the intervention group 28 (70%), although not significant for the Bonferroni adjusted α of 0.007. The overall

mean target score of 7.1 out of 9 (p=0.0001) achieved by the intervention group was significantly greater than the score of 4.8 achieved by the control group.

Table 4.2

Comparison of Proportion of Targets Achieved

Target achieved	**Primary propensity matched model : eGFR, age, sex, diabetes, donor**		
	Intervention N=40 (%)	Control N=40 (%)	P-value
Systolic Blood Pressure	26 (65)	21 (53)	0.33
Diastolic Blood Pressure	35 (88)	30 (75)	0.23
Calcium	35 (88)	19 (51)	0.004
Carbon dioxide	28 (70)	37 (95)	0.02
Hemoglobin	30 (75)	35 (88)	0.30
Low density lipoprotein	31 (78)	6 (18)	0.006
Phosphate	36 (90)	34 (85)	0.62
Parathyroid hormone (PTH)	29 (74)	6 (18)	*0.006
Mean Target Score(+/-SD)	7.1 +/- 3.1	4.8+/- 1.4	0.0001

Chi square test to compare proportions, Student's t-test to compare means, p-values two-tailed, Bonferroni corrected $\alpha = 0.007$ *Fischer exact test

Comparison of the mean target values. The mean value for LDL was within the target range (< 2.6 mmol/L) for the intervention group (2.2 +/- 0.77) and above the target range in the control group (3.4 +/- 0.81) (see Table 4.3). This difference was statistically significantly (p=0.0001). Calcium and carbon dioxide means were significantly different, but remained within the target ranges. Blood pressure mean values were not significantly different between the two groups, although were below the target range (≤ 140) for the control group and above in the intervention group (≤ 130).

Table 4.3

Comparison of Mean Target Values

Primary propensity matched model: eGFR, age, sex, diabetes, donor			
Target (range)	Intervention (n=40)	Control (n=40)	P-value
Systolic blood pressure mmHg (≤ 130 treatment/ ≤ 140 control)	133 ± 13.6	139 ± 16.3	0.09
Diastolic blood pressure mmHg (≤ 80 treatment/ ≤ 90 control)	77.3 ± 7.9	80.2 ± 8.3	0.11
Calcium (2.23 – 2.58 mmol/L)	2.4 ± 0.13	2.3 ± 0.15	0.0001
Carbon dioxide (21-32 mmol/L)	22.1 ± 2.9	24.2 ± 2.8	0.002
Hemoglobin (105-120 g/L)	110 ± 11.5	119 ± 14.8	0.10
Low density lipoprotein (<2.6 mmol/L)	2.2 ± 0.77	3.4 ± 0.81	0.0001
Phosphate (0.6 – 1.80 mmol/L)	1.4 ± 0.31	1.3 ± 0.3	0.11

Means ± SD, p-values-Student's t-test, Bonferroni corrected α=0.007

Secondary Outcome Results

Use of health care services. The use of health care services, in the intervention and control groups, was compared using the incidence rate ratio (IRR); there was a significant difference between the groups in the rate of emergency department visits and hospital admissions. The control group had a significantly greater rate of visits (IRR 0.53, p=0.02) and admissions (IRR 0.34, p=0.001), as compared to the intervention group over the 12-month study period (see Table 4.4).

Table 4.4

Use of Health Care Services in 12 Months

Health service (All cause)	**Intervention** (n=40)	**Control** (n=40)	**IRR**	**95% CI**	**P-value**
Emergency visits	21	40	0.53	0.29, 0.91	0.02
Hospital admissions	12	35	0.34	0.16, 0.68	0.001

p-values based on incidence rate ratio (IRR), upper bound on rate ratio <1.0, significant at p= 0.05, CI = Confidence Interval

Process implementation. The process measures used in this study included measures reflective of applying a standard of practice based on existing evidence. A significantly greater proportion of intervention patients received ASA, ESA, ACE-I /ARB, statins, calcium supplements, and calcitrol as compared to the control group. No significant difference was found between the proportions of patients who had measurements of laboratory values for LDL, calcium or phosphate. PTH was measured in a significantly greater proportion (p=0.0001) of intervention patients 38 (95%) as compared to the control group 6 (15%). No significant difference was found between the mean numbers of clinic visits per year in each group (see Table 4.5).

Table 4.5

Proportion of Achieved Process Measures

Propensity-score model: matched for eGFR, age, sex, diabetes, kidney donor

Process measure	Intervention n=40 (%)	Control n=40 (%)	P-value
Standard treatment			
ASA	20 (50)	9 (23)	0.01
ESA	26 (65)	13 (33)	0.006
ACE-I/ARB	21 (53)	5 (13)	0.004
Statin	32 (80)	18 (45)	0.004
Calcium	29 (73)	10 (25)	0.0001
Calcitrol	26 (65)	7 (18)	0.0002
Tests			
Low density lipoprotein (LDL)	34 (85)	33 (83)	0.76
Parathyroid hormone (PTH)	38 (95)	6 (15)	0.0001
Calcium	40 (100)	37 (93)	0.24
Phosphate	40 (100)	37 (93)	0.24
Clinic visits (mean)	7.1	6.9	0.64

Chi square test used to compare proportions; p-values two-tailed,
Bonferroni corrected $\alpha = 0.005$; ASA=acetylsalicylic acid; ESA=Erythropoiesis-stimulating agent; ACE-I= angiotensin-converting enzyme inhibitor; ARB=angiotensin receptor blocker

Propensity-score matching. An additional secondary study objective was to determine whether matching based on the propensity-score method, to adjust for the non-randomized nature of this study, results in a balanced distribution of the co-variates eGFR, age, sex, diagnosis of diabetes and kidney donor type (e.g., living versus deceased). Prior to propensity-score matching, the intervention patients had significantly lower eGFR (20 +/- 5.1 versus 27 +/- 6.4, $p<0.0001$), were similar in the proportion receiving a living kidney donor, similar in age, sex, diagnosis of diabetes, and the amount of time since transplant (see Table 4.0) as compared to the control group. A significantly greater proportion of patients in the intervention group (n=61), had the diagnosis of hypertension ($p=0.05$) or immunoglobulin A nephropathy ($p=0.004$) as the primary cause of their ESRD as compared to the control group (n=119). Figure 4.1 provides a graphical representation of the covariate balance pre and post propensity-score matching, showing a SD +/- 20 after matching. The inclusion of the chosen co-variates resulted in an equal distribution of the included co-variates between the propensity-matched groups.

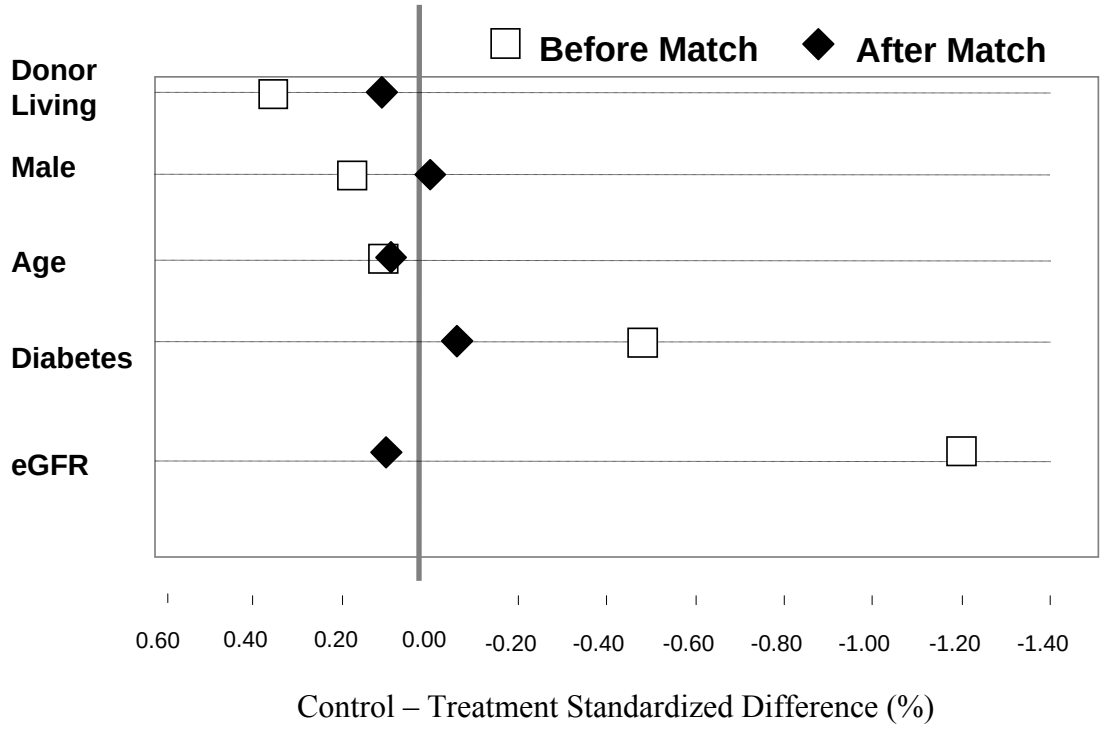

Figure 4.1 The covariate balance pre and post propensity-score matching.

Alternate propensity-score matching models were developed to determine if matching on fewer co-variates resulted in an equal distribution of variables between the two groups and influenced the outcomes (see Table 4.6). In the first alternate propensity-score model, using only eGFR as a covariate, a significantly different distribution was found for the proportion of males, 30 (68%) in the intervention group as compared to 20 (46%) in the control group ($p=0.03$), and proportion of intervention patients with hypertension as the primary cause of their end-stage renal disease ($p=0.05$). In the second alternate propensity-score model, using eGFR, age, and sex as co-variates, a significantly different distribution was found between the proportion of patients with hypertension, glomerular nephritis, immunoglobulin A nephropathy, and unknown as the primary cause of their end-stage renal disease ($p<0.05$)

Table 4.6

Alternate Propensity-Score Matched Models and Baseline Characteristic Comparison

Baseline characteristics	**Primary model** eGFR, age, sex, donor type, diabetes			**Model 2** eGFR			**Model 3** eGFR, age, sex,		
	I (%) (n=40)	C (%) (n=40)	P-value	I (%) (n=44)	C (%) (n=44)	P-value	I (%) (n=44)	C (%) (n=44)	P-value
Age- years	51 ± 15	50 ± 14	0.69	51 ± 14	50 ± 15	0.80	51 ± 15	52 ± 14	0.72
eGFR mL/min/1.73 m²	21 ± 5.1	21 ± 6.1	0.80	21 ± 5.5	21 ± 5.8	0.98	21 ± 5.1	21 ± 6.1	0.97
Time since last transplant- months	130 ±95	109± 91	0.32	124 ± 77	109 ± 93	0.42	137 ± 106	119 ± 100	0.44
Male, %	60	60		30 (68)	20 (46)	0.03	28 (64)	28 (64)	
Diagnosis of Diabetes	9 (23)	10 (25)	0.79	10 (23)	6 (14)	0.27	9 (21)	10 (23)	0.80
Living Kidney Donor, %	14 (35)	12 (30)	0.63	13 (30)	11 (25)	0.63	15 (34)	9 (21)	0.15
End-Stage Renal Disease Etiology									
Diabetes	9 (23)	10 (25)	0.79	10 (23)	6 (14)	0.28	9 (21)	10 (23)	0.82
Polycystic kidney	4 (10)	4 (10)		4 (9)	7 (16)	0.32	4 (9)	4 (9)	
Glomerular nephritis	5 (13)	11 (28)	0.09	9 (21)	14 (32)	0.25	7 (16)	15 (34)	0.05
Hypertension	3 (8)	0 (0)	0.27	4 (9)	0 (0)	0.05	4 (9)	0 (0)	0.05
Interstitial nephritis	2 (5)	1 (3)	0.64	2 (5)	1 (2)	0.45	2 (5)	1 (2)	0.45
Obstructive reflux	3 (8)	3 (8)		1 (2)	4 (9)	0.15	4 (9)	2 (5)	0.46
Lupus	0 (0)	2 (5)	0.16	0 (0)	3 (7)	0.08	0 (0)	2 (5)	0.14
Drug induced	1 (3)	0 (0)	0.27	1 (2)	0 (0)	0.35	2 (5)	1 (2)	0.45
Vasculitis	0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	1 (2)	0.35
Congenital renal dysplasia	5 (13)	5 (13)		7 (16)	4 (9)	0.32	7 (16)	3 (7)	0.19
IgA nephropathy	3 (8)	0 (0)	0.07	3 (7)	0 (0)	0.08	4 (9)	0 (0)	0.05
Pyelonephritis	1 (3)	0 (0)	0.27	1 (2)	0 (0)	0.35	0 (0)	0 (0)	
Unknown	2 (5)	4 (10)	0.34	1 (2)	5 (11)	0.09	1 (2)	5 (11)	0.05
Other	2 (5)	0 (0)	0.16	1 (2)	0 (0)	0.35	0 (0)	0 (0)	

I=intervention, C=control, IgA=immunoglobulin A

p-values from Student's t-test for continuous variables, reported as mean +/- standard deviation; Chi square test for categorical variables,

All reported p-values 2-tailed, significant $p \leq 0.05$; eGFR=Glomerular filtration rate calculated using the abbreviated MDRD study equation (Levey et al., 1996).

Propensity-score model and outcomes. In addition to determining if the co-variates chosen for each propensity-model equally controlled for distribution between the groups, this study also measured and compared the primary outcomes based on the three propensity-score models (see Table 4.7). A comparison of the three propensity-score models and primary outcomes found no differences in the results associated with each model, except for the PTH target, which was only significant in the primary propensity-score model. The statistically significant results were consistent across the three models.

Table 4.7

Outcomes by Propensity-Score Model

	Primary propensity-score model			**Propensity-score eGFR**			**Propensity-score eGFR, age, sex**		
Target achieved	I n=40 (%)	C n=40 (%)	P Value	I n=44 (%)	C n=44 (%)	P value	I n=44 (%)	C n=44 (%)	P-value
Target Score of 78%	27(68)	4(10)	0.0001	28(64)	3(7)	0.0001	28(64)	3(7)	0.0001
ESRD Discussion	35(88)	5(13)	0.0001	39(89)	5(11)	0.0001	38(86)	5(11)	0.0001
Systolic BP	26(65)	21(53)	0.33	31(71)	23(52)	0.08	30(68)	22(50)	0.08
Diastolic BP	35(88)	30(75)	0.23	38(86)	34(77)	0.27	38(87)	35(80)	0.4
Calcium	35(88)	19(51)	0.004	38(86)	19(48)	0.0008	37(84)	22(55)	0.005
Carbon dioxide	28(70)	37(95)	0.02	32(73)	39(91)	0.03	32(73)	40(93)	0.02
Hemoglobin	30(75)	35(88)	0.30	32(73)	35(80)	0.45	34(77)	37(84)	0.42
Low density lipoprotein	31(78)	6(18)	0.006	33(75)	8(22)	0.0001	33(75)	7(19)	0.0001
Phosphate	36(90)	34(92)	0.62	37(84)	38(93)	0.3	38(86)	36(90)	0.72
PTH	29(74)	6(18)	*0.006	30(75)	8(100)	*0.47	31(74)	7(100)	*0.47

I=Intervention group, C=Control, ESRD=End-stage renal disease, BP=Blood pressure, PTH=Parathyroid hormone, *Fischer exact test used when cells had less then five individuals
Chi square test to compare proportions, p-values two-tailed, Bonferroni corrected $\alpha = 0.007$

Medication adherence behaviour and target score achievement. An additional secondary objective was to determine the association between patient-reported medication non-adherence events and achievement of the target score. The proportion of intervention patients who achieved the targets was compared based on those with or without documented reports of non-prescribed adjustment of medications. Of the 61 intervention patients, 18 (30%) had no reports of medication non-adherence and 43 (70%) reported 152 medication non-adherence events, with a range of 1 to 9, mean of 3.5 and median of 3 over 1 year (see Table 4.8). The patient reports on non-adherence included any missed, changed or discontinued medication. There was no statistically significant difference in all but one target, between the groups. The carbon dioxide target was achieved by a higher proportion, 16 (89%, p=0.04), of medication adherent patients, although not significant when Bonferroni corrected for $\alpha = 0.005$.

Table 4.8

Medication Non-Adherence and Target Achievement in the Intervention Group (N=61)

Target	**No reported medication non-adherence*** n=18 (%)	**Reported medication non-adherence*** n=43 (%)	**P-value**
Systolic BP	13 (72)	28 (65)	0.59
Diastolic BP	16 (89)	37 (86)	1.00
Hemoglobin	13 (72)	31 (72)	0.99
Low-density lipoprotein	15 (83)	31 (72)	0.52
Parathyroid hormone	13 (77)	28 (73)	1.00
Calcium	16 (89)	35 (81)	0.71
Phosphate	17 (94)	36 (84)	0.42
Carbon dioxide	16 (89)	27 (63)	0.04
End-stage renal disease options discussed	14 (78)	41 (95)	0.06
Target score 7/9	15 (83)	25 (52)	0.06

BP=Blood pressure, p-values two-tailed, Chi-square tests (Fischer where appropriate), Bonferroni corrected $\alpha = 0.005$

* all prescribed medications including immunosuppressants

Measuring the dose of chronic disease management interventions. The dose of chronic disease management intervention (CDM) was measured for all patients in the full intervention group (n=61), to permit the analysis of the effect of dose on outcomes. Intervention user rates were calculated for each healthcare professional. Of the 1661 documented entries reflecting a chronic disease management (CDM) intervention unit of delivery for the intervention group (n=61), patients received 56% of the total CDM intervention from the APN, thus equivalent to an intervention user rate of 10.3 units per patient per clinic visit. The patients received 3% of the CDM intervention from the physician, 20% from the pharmacist, 16% from the dietitian, and 5% from the social worker. The total intervention user rate, when combining all health professionals, was 18.42 units per patient per clinic visit, which represents a measure of the CDM intervention delivery dose per patient (see Table 4.9).

Table 4.9

Chronic Disease Management (CDM) Intervention User Rates (N=61)

Health professional	**Amount*** mean # of CDM documentations	**Frequency**** mean # of clinic visits over 12 months	**Intervention user IUR** (IUR)***	**Proportion of total IUR**
APN	15.3 (934/61)	8.1	10.3	56%
Physician	0.7 (41/61)	8.1	0.50	3.0%
Pharmacist	5.5 (333/61)	8.1	3.71	20%
Dietitian	4.3 (264/61)	8.1	2.90	16%
Social Worker	1.5 (89/61)	8.1	1.01	5.0%
Total	**27.3 (1661/61)**	**8.1**	**18.42**	**100%**

* amount = unit of CDM intervention delivery = documentation in patient chart
** frequency = number of times intervention delivered over 12 month study period
*** strength of intervention (amount x frequency/12 months);
APN-Advanced practice nurse

To determine the effect of the CDM intervention dose on target achievement, the mean intervention dose for patients who achieved the targets and those who did not was compared (see

table 4.10). A significantly greater mean dose of intervention (3.9 versus 2.2, p=0.0001) was received by those patients who participated in discussions on end-stage renal disease options, as compared to those who did not. No significant difference was found in mean dose between those patients who achieved the remaining six targets as compared to those who did not.

Table 4.10

Effect of Intervention User Rate Mean Dose on Target Achievement (N=61)

Outcomes- achieved targets			**Mean "dose"- IUR**		**P-value**
	Yes (%)	No (%)	Yes (SD)	No (SD)	
Target score					
7 or more targets of 9	40 (66)	21 (34)	3.65 (1.53)	3.92 (1.43)	0.50
Systolic BP	41 (67)	20 (32)	3.64 (1.40)	3.94 (1.81)	0.47
Diastolic BP	53 (89)	8 (11)	3.66 (1.40)	4.27 (2.03)	0.28
Hemoglobin	44 (72)	17 (28)	3.83 (1.50)	3.50 (1.48)	0.44
Low-Density Lipoprotein	46 (75)	15 (25)	3.72 (1.52)	3.81 (1.41)	0.85
Parathyroid Hormone	43 (71)	18 (29)	3.57 (1.42)	4.16 (1.61)	0.16
Calcium	51 (84)	10 (16)	3.66 (1.43)	4.16 (1.77)	0.33
Phosphate	53 (89)	8 (11)	3.70 (1.55)	4.01 (1.04)	0.59
Carbon Dioxide	43 (71)	18 (29)	3.65 (1.46)	3.96 (1.57)	0.44
ESRD Options Discussion	55 (90)	6 (10)	3.91 (1.46)	2.15 (0.53)	0.0001

BP = Blood Pressure, ESRD=End-Stage Renal Disease, p-values from Student's t-test, Bonferroni corrected $\alpha = 0.005$; Mean dose reported +/- standard deviation (SD), IUR = intervention user rate

Chapter Five

Discussion

The TARGET study is the first known study evaluating the effectiveness of an APN led inter-professional collaborative chronic care approach on the achievement of targeted clinical outcomes and the implementation of recommended processes of care (K/DOQI practice standards) for patients with kidney transplant CKD. The evaluation of the TARGET study showed that patients exposed to the APN led approach (a) are more likely to attain the targeted clinical outcomes, (b) are more likely to participate in discussions about ESRD options, (c) have fewer hospital admissions and emergency department visits; and (d) are more likely to have K/DOQI standards implemented in their care. While the primary propensity-score method for matching was the only one that resulted in equivalent baseline characteristics between groups, there were no differences between the three propensity scoring models in the findings related to the primary outcomes of this study. The results that did not support the TARGET study's original hypotheses included (a) patients reporting medication non-adherence events did not achieve fewer clinical targets as compared to adherent patients, and (b) patients achieving clinical targets did not receive a higher mean dose of chronic disease management intervention as measured by the intervention user rate (IUR).

The selected group of kidney transplant CKD patients is a unique subset of the kidney transplant population, known to be at higher risk for the complications and co-morbidities associated with the progression of CKD and failing kidney graft (Gill et al., 2004). The results of this study indicated that a multifaceted, inter-professional, APN-physician, collaborative care approach could increase the proportion of patients achieving the targeted clinical goals and

increase the number of discussions held with patients on treatment options for end-stage renal disease as compared to patients within the traditional approach to kidney transplant care.

Very few nursing studies have applied a propensity-score matching analysis when an RCT is not feasible (Qin et al., 2008). The propensity-score method was chosen for use in this study to match those who received the intervention to those who did not. It was then possible to infer a stronger causal association for the intervention effect because the patients in the matched samples had a similar likelihood of receiving care within the APN led inter-professional collaborative chronic care clinic. An additional value of this study to nursing research was the calculation of an intervention user rate, which provided an objective approach for examining and measuring the dose of chronic disease management provided by healthcare professionals to this patient population.

The patients in this study were similar to those reported in other studies involving kidney transplant CKD populations in terms of age, sex, type of kidney donor (Djamali et al., 2003; Karthikeyan et al., 2003), diagnosis of diabetes, and time since kidney transplant (Akbari et al., 2007). The proportion of study patients with hypertension, polycystic kidney disease or glomerular nephritis, as the primary cause of ESRD, was similar to those reported in the literature for kidney transplant populations (CIHI, 2010). The mean age of the study patients was 51.5 years, similar to those reported in the literature for the Canadian kidney transplant population (CIHI, 2010), although slightly older than those reported in a U.S. study of failed kidney transplants (43 +/- 12 years) or stage five CKD (Gill et al., 2002). The proportion of Canadian kidney transplant recipients older than age 60, receiving a transplant from a deceased donor, increased from 18 to 36 percent since 1999, with the average age increasing from 47.8 to 53.2 years (CIHI, 2010). A similar trend exists for living donor transplants (10% to 19%), with the

average age increasing from 42.6 to 46.8 years. These Canadian trends may account for the slightly older age of our study sample.

In summary, the patients in this study were similar to those reported in other studies of kidney transplant populations in age, sex, cause of ESRD, time since transplant and type of kidney donor. It is important to note that there is a paucity of literature describing the kidney transplant stage four and five CKD populations. While the study sample was slightly older than the reported age of failed kidney transplant patients in one U.S. study, it was comparable to the mean age of the overall Canadian kidney transplant population (CIHI, 2010; Gill et al., 2002). Overall, the patients in this study appear representative of kidney transplant stage four and five patients.

Primary Research Question

The primary research question was, is there an association between patients' exposure to an APN led inter-professional collaborative chronic care approach and achievement of clinical targets and discussions about end-stage renal disease options? The findings suggest patients exposed to the APN led approach are more likely to achieve the target score and participate in discussions about end-stage renal disease options. Compared to the control group, the patients in the APN led clinic achieved the target score (68% versus 10%) and participated in discussions related to end-stage renal disease options (88% versus 13%).

These study results are consistent with the results found in a similar study comparing an inter-professional CKD clinic care approach for progressive CKD patients to traditional kidney transplant care for kidney transplant CKD patients (Akbari et al., 2007). Akbari (2007) found significant differences in the management of CKD between the above two patient populations. The kidney transplant CKD population were less likely to achieve the targets for blood pressure, lipids, and anemia as compared to the non-transplant CKD population. Moreover, the non-

transplant CKD population, followed by an inter-professional care team with a CKD focus, were more likely to participate in discussions on their ESRD options and have a dialysis plan in place, as compared to the kidney transplant CKD patients (7%) (Akbari et al., 2007). The TARGET study results suggest a similar approach to health care, with the addition of the APN role increases the likelihood of end-stage renal disease options discussions with kidney transplant CKD patients. However, the Akbari et al. (2007) study did not include an APN, or compare equivalent groups in terms of baseline characteristics, and therefore may in part limit comparison or generalization to the TARGET study.

Results of the TARGET study for the individual clinical outcomes showed a significantly greater proportion of the intervention group achieved the low-density lipoprotein, calcium, and PTH target, as compared to the controls. There was no significant difference between the proportions in each group achieving the targets for blood pressure, phosphate or hemoglobin levels. There are several explanations for the lack of significant differences in individual targets found in this study. First, the lack of significance may be explained in part by the small sample size. The sample size calculation for this study was based on the primary outcome of a target score as opposed to individual targets. The resulting sample size for the individual targets in each group was underpowered to detect a significant difference. Of the intervention patients, 26 (65%) achieved the systolic blood pressure target and 35 (88%) achieved the diastolic blood pressure target, as compared to 21 (53%) and 30 (75%) of the control group. This corresponds to a standardized difference of .24 for systolic blood pressure. Based on this difference, the study had only approximately 15% power to detect a difference of this size using the cut-off for statistical significance of 0.05. A sample size of approximately 260 in each group would have been required to detect a significant difference in systolic blood pressure at a power of .80. A similar calculation

would find the resulting sample sizes in diastolic blood pressure, phosphate and hemoglobin targets underpowered.

A second explanation for the lack of significant difference in blood pressure and hemoglobin target achievement in the intervention group as compared to controls relates to the risk and concern of exacerbating hypertension with the use of erythropoietin stimulating agents (ESAs) (Gill et al., 2002; Karthikeyan et al., 2003). The mean systolic blood pressure increases with each stage of CKD and concurrently the mean hemoglobin decreases with each stage. At stages four and five CKD, it is common for kidney transplant patients to be taking three or more anti-hypertensive agents, yet continue to experience uncontrolled blood pressure (Karthikeyan et al., 2003). Third, randomized controlled trial evidence on the optimal hemoglobin range and use of ESAs for the treatment of anemia is limited for the kidney transplant CKD population, and may in part have led to decreased usage of this medication. Akbari et al., (2007) reported similar results, where no significant differences were found between the non-transplant CKD and transplant CKD patients' systolic blood pressure and hemoglobin targets; however, phosphate was not measured in this study.

A major difference in the TARGET study approach to health care, which may partly account for the significant achievement in target score in the intervention group, was the organization of care guided by the CCM and the use of an APN led collaborative inter-professional healthcare team. The optimization of clinical outcomes for the kidney transplant CKD patients in this study is consistent with the results of similar studies evaluating the implementation of APN led chronic disease approaches to health care. The studies of APN led chronic disease management have included patients with conditions such as chronic obstructive pulmonary disease, diabetes, hypertension, CKD, congestive heart failure and Alzheimer disease (Graham et al., 2006; Litaker

et al., 2003; Wong et al., 2005). The results of these studies indicated that an APN led approach (a) significantly increased the targeted health outcomes such as blood pressure, diabetes control, screening for nephropathy and retinopathy, and home glucose monitoring among patients with diabetes (Graham et al., 2006; Litaker et al., 2003; Wong et al., 2005); and (b) significantly reduced re-hospitalization and acute care rates among patients with chronic obstructive pulmonary disease or congestive heart failure (Felber-Neff et al., 2003; Naylor et al., 2004). More specifically patients with CKD exposed to the APN led care were shown to have optimized hemoglobin, the use of erythropoiesis stimulating agents, and dietary counselling (Harwood et al., 2004; Lee et al, 2007). A systematic review of nurse led interventions to improve the control of blood pressure in people with hypertension indicated the use of an algorithm to structure care resulted in greater reductions in systolic blood pressure (-8.2mmHg, 95% CI -11.5 to -4.9) as compared to usual care (Clark, Smith, Taylor, & Campbell, 2010). The TARGET study is the first study to evaluate the implementation of an APN led inter-professional chronic disease approach to health care for kidney transplant CKD patients.

Historically, a major focus for kidney transplant care has been on immunosuppression management and efforts to maintain kidney graft function (Gill et al., 2002). Moreover, the traditional transplant clinic includes all post kidney transplant patients with normal renal function and all stages of CKD or acuity (Gill et al., 2002), whereas the TARGET study only focused on those kidney transplant patients with CKD stages four and five. The focus on immunosuppression, the monitoring and follow-up of new kidney transplant patients and those with acute health care needs may divert attention from the management of the co-morbidities and complications associated with kidney transplant CKD, as well as the planning required for those with end-stage renal disease (Akbari et al., 2007; Gill et al., 2002). Therefore separating this more complex care

population from all post kidney transplant patients and enhancing their organization of care with APNs is a better approach as demonstrated in the TARGET study.

Wagner (1998) suggests that healthcare professionals, using a tertiary or acute care approach, focused solely on the primary reason for the visit and have a limited amount of time for the encounter, which results in a lack of long-term or chronic disease management. Although the immediate health concern may be addressed in the healthcare visit, the underlying issues associated with chronic disease management may go unattended (Anderson & Knickman, 2001). The TARGET study results suggest that the combination of care led by an APN, organized around the chronic care model, and the implementation of protocols based upon evidence to support best practices among healthcare professionals for kidney transplant CKD patients may enhance the achievement of the clinical target goals associated with CKD management.

Secondary Research Questions

Utilization of healthcare services. An important secondary finding in the TARGET study was the significant reduction in total number of emergency department visits (21 versus 40) and all cause hospitalizations (12 versus 35) in the intervention group as compared to controls, over the 12-month study. A costing of this reduction in healthcare service use by the intervention patients based on the standardized interprovincial rate for one emergency department visit ($247.00) and one overnight hospital admission ($1,163.00) per patient converts to a savings of $26,749.00 in total number of hospital admissions, based on one overnight stay per admission, and $4693.00 in total ER visits. A conservative estimate, in the intervention group (n=40), of a three-day length of stay for kidney transplant CKD patient admissions converts to $80,247.00 potential savings to the healthcare system in the control group of 40 as compared to the intervention group.

The Ministry of Health, Ontario Joint Policy and Planning Committee (JPPC, 1997), funding formula for the ambulatory CKD clinic care of patients with stage 4 or greater CKD (eGFR $\leq$ 30 ml/min/1.73m^2) is at a higher rate when the healthcare team includes two or more healthcare professionals, in addition to the physician (e.g., APN, dietitian, social worker or pharmacist). The funding rate for each clinic appointment, for kidney transplant patients with stage 4 CKD or greater and seen by an inter-professional healthcare team, is $240.00 as compared to $90.00 for those patients with CKD stages 1 to 3, and not seen by an inter-professional healthcare team. Based on the mean number of clinic appointments (7.1) for the intervention patients (n=40) in the TARGET study, remuneration for the healthcare service over the 12-month study was $68,160.00 as compared to $24, 840.00 (6.9 X 40 X $90.00) for the control group. The above costing represents an increase in hospital funding of $43,320.00 per year for the intervention group (n=40) or $1083.00 per patient, and a cost savings of up to $84,940.00 per year, or $2123.50 per patient, based on a 3-day length of hospital stay.

DiCenso and Bryant-Lukosius (2010), in a recent report on Clinical Nurse Specialists and NPs in Canada, identified inadequate funding as a recurrent issue for healthcare organizations wishing to implement APN positions. One reason cited for this was the economic downturn, which administrators stated directly affected available funding for existing or future APN positions (DiCenso & Bryant-Lukosius, 2010). The results of the TARGET study, which demonstrate a reduction in health care service use, provides an estimate of the impact of an APN led approach on health care costs in one select patient population and health care setting. Evidence on the cost benefit for APN roles is lacking and researchers are unable to generalize the cost benefit across differing settings or patient populations (Clark et al., 2010; Kinnersley et al., 2000). Quantifying the impact reinforces the value that the APN role adds and represents a potential long-term

evaluation approach to support the needed stability and sustainability of APN roles (DiCenso & Bryant-Lukosius, 2010).

Implementation of evidence-based practice standards. The CCM, as the conceptual framework that guided this study's intervention, also served as a guide to the evaluation of the study results. To assess the quality of health care in the management of kidney transplant patients with CKD, it is essential to relate the structure and processes of care to the patient outcomes.

The structure and process of chronic care. The components of the CCM that reflected structural elements in the study framework were (a) a CKD focus (the health system organization), (b) an APN-physician collaborative inter-professional healthcare team (the delivery system design), and (c) a patient centered collaborative care approach for disease self-management. Based on these structural elements, a comparison of the traditional approach and APN led approach revealed key differences in the organizational features and clinical practice implementation patterns that may in a large part, account for the improvement in target achievement and patient outcomes in the intervention group. The difference in organizational features included (a) clinic appointment length and frequency, and (b) differences in the continuity of the type of healthcare professionals involved in the patients care.

The patients in the intervention group had longer and more frequent clinic visits, which included a health management assessment by an APN, pharmacist, dietitian, social worker and the transplant nephrologist as required. The structural change, that facilitated this approach, was the dedicated clinic and inter-professional staff members for the care of kidney transplant CKD patients scheduled concurrently with a kidney transplant non-CKD patient clinic. Over the 12-month period, the healthcare professional team assessed intervention patients in the clinic a mean of 8.13 times, with the APN spending 58% of that time with the patient on chronic disease focused

interactions. The same team of healthcare professionals, assessed patients at each clinic visit. Each clinic visit lasted an average of 40 minutes. The one exception to this team was the change in transplant nephrologist due to the continued weekly rotation of physicians for the transplant clinic. In addition, the weekly inter-professional, patient-focused team meetings supported continuity of care for patients through the sharing of patient related goals and updates.

In contrast, the control group patients were seen in the clinic a mean of 6.3 times over the 12 month study period with one of four transplant nephrologists or the attending nephrology resident providing medical care, along with one of four clinic RNs. The healthcare team did not include a pharmacist, and assessment by a dietitian or social worker did not occur in a standardized fashion. Each clinic visit lasted an average of 20 minutes. Formal team meetings did not occur for the control group. A transplant clinic dedicated to CKD management may contribute to an improvement in the coordination and delivery of chronic health care, as well as important services such as standardized medication reviews, dialysis options education, nutritional counselling and social work that are specific to the needs of kidney transplant CKD patients.

Further study of the impact of the intensity of long-term follow-up, continuity of care and the regular conduct of inter-professional patient care meetings, as they relate to outcomes in the kidney transplantation population, is required (Akbari et al., 2007). In a recent Cochrane collaboration review (Zwarenstein et al., 2009) the authors suggested that the addition of inter-professional interventions (i.e., patient rounds and team meetings) could enhance healthcare processes and outcomes. In this review, as in the TARGET study, the authors were unable to infer which components of the inter-professional collaborative team approach contributed to improvements in healthcare processes and patient outcomes. However, the TARGET study results did indicate a significant difference in the processes (e.g., implementation of recommended

standards and use of medical directives) of kidney transplant chronic kidney care, as they relate to provision of care by an inter-professional team, which may explain, in large part, the optimization of the intervention patient's outcomes.

An interesting finding in this study was the difference in the proportion of intervention and control patients for which healthcare professionals implemented the recommended treatment. Clinical practice standards and evidence-based guidelines are increasingly common in healthcare (Grimshaw et al., 2004). In the kidney transplant CKD population, evidence based guidelines are based primarily on practice recommendations developed for the non-transplant CKD population (NKF, 2002; 2003; 2003a; 2004). Those guidelines that have been developed for the kidney transplant patients focus largely on the non–CKD transplant population with recommendations for monitoring and managing immunosuppressant therapy, treatment of rejection, monitoring kidney function, risk for and treatment of infectious disease, malignancy and cardiovascular disease (KDIGO, 2009; NKF, 2004a; 2006).

In the TARGET study there was a significant difference in the proportion of intervention patients who received the recommended standard of care for hyperlipidemia (e.g., statin medications, 78 versus 18%), bone metabolism (e.g., calcium supplements, 73 versus 25%; calcitrol, 65 versus 18%), anemia (e.g., erythropoiesis stimulating agents, 65 versus 33%), cardiovascular disease and stroke prevention (e.g., ASA, 50 versus 23%), and hypertension (e.g., ACE-I/ARBs, 44% versus 10%). In contrast, no statistical significant difference was found between the groups for the screening of LDL, calcium and phosphate levels. A possible explanation for the differences found in the TARGET study may be the use of a formalized, kidney transplant CKD protocol, in the form of medical directives, to guide clinical treatment decision making for the APN. The formalized protocol provided guidance on treatment based on laboratory

values. Despite the testing of LDL, calcium and phosphate levels in the control group, these targets remained suboptimal, suggesting an even greater role for the use of formalized protocols in this setting.

Grimshaw (2004), in a systematic review of guideline dissemination and implementation strategies to improve the processes of care, found that the implementation of guideline reminders promoted healthcare professional compliance with the recommended practices. In this review, reminders were defined as "patient or encounter specific information, provided verbally, on paper or on a computer screen, which are designed to prompt a health professional to recall information" and "so remind them to perform some action to aid individual patient care" (Grimshaw et al., p. 8, 2004). The medical directives used in the TARGET study served as a prompt to the APN about the recommended kidney transplant CKD preventative and treatment strategies. In addition, the inter-professional patient care meetings provided the opportunity to interact with peers and discuss individual patient care recommendations and relevant guidelines as verbal reminders to the healthcare team (Grimshaw et al., 2004). In the TARGET study, it was unclear, to what degree physicians in the traditional clinic referred to relevant practice recommendations or what strategies they used to prompt or consider implementation of these standards in the practice setting.

In summary, although Wagner (2000) developed the CCM for use in the primary care setting, the TARGET study results suggest that it appears to be valid for use in this tertiary ambulatory care setting. The combined use of an intervention based on the CCM, with the delivery of care by an APN led collaborative inter-professional healthcare team, and standardized protocols to guide the organization and structure, improves the processes of care, patient outcomes, and the overall quality of transplant CKD patient care. In large part, these differences may explain the improved outcomes in the patients followed in the chronic kidney care renal transplant clinic.

Propensity-score analysis. Another secondary research question related to the use of propensity-score matching. The question was does a propensity-score matching model based on selected variables control for the differences in co-variates between the intervention and control groups? The associated hypothesis was to determine if the use of alternate propensity-score matching models influenced the primary outcome results.

Co-variate equivalency. Although, three propensity-score models were developed to vary the co-variates, there was no difference on the primary outcomes between the intervention and control groups. However, primary propensity-score matching appeared to be best, given the equal distribution of variables between the intervention and control groups. Moreover, an equal distribution was found also for the time since transplant and primary cause of ESRD, although not included as co-variates. In kidney transplant patients, hypertension is a significant risk factor for cardiovascular disease and chronic kidney graft dysfunction (Kasiske et al., 2004; Mange, Cizman, Joffe, & Feldman, 2000). As such, the validity of outcomes could be questioned if baseline characteristics included an unequal distribution of hypertension as the primary cause of ESRD due to its potential influence on the outcomes that occurred in the propensity-score matching that used eGFR alone.

In the propensity-score matched model with eGFR, age and sex, there was a significant difference ($p=0.05$) between the two groups in the proportion of patients with glomerular nephritis, hypertension, IGA nephropathy or unknown as the primary cause of their ESRD. In this model, as with eGFR alone, the primary causes of ESRD are related to achievement of clinical outcomes, and in some situations, influence disease progression based on the degree of proteinuria associated with the underlying disease. An increase in proteinuria is a risk factor for a more rapid progression

of kidney dysfunction, and as such negatively influences the optimization of clinical outcome targets such as blood pressure and hemoglobin.

Brookhart et al. (2006) suggest that for small studies, when identifying variables to include in the propensity-score models, those variables strongly related to the intervention but weakly related to the outcome remove only a small amount of bias. In the TARGET study, eGFR was the variable strongly related to the intervention, whereas the variables strongly related to the outcomes were donor type and the presence of diabetes. Interestingly, in the TARGET study, the addition of more variables did not change the significantly improved outcomes in the intervention group. The majority of researchers, reporting the use of a propensity-score model for matching, conduct their studies with very large sample sizes to reduce the risk of a type two error (Austin, 2007; 2008). The difficulty for the researcher is in identifying which of the patient variables to include in the propensity-score model, as the bias and variance of the estimated intervention effect is dependant on this selection. The addition of variables beyond eGFR resulted in no increase in the variance of intervention effects, which may suggest that, in the kidney transplant CKD population, eGFR can be used as the single co-variate for matching in a propensity-score model when randomization is not feasible.

Impact on primary outcomes. Despite the study hypothesis, which stated the outcomes would differ when the full primary propensity-matched model was used, the TARGET study results did not differ. This may lead one to suggest, the full model is not needed and inclusion of the variables age, sex, donor type, and diabetes is not necessary. The baseline patient characteristics are potential confounders that can be both predictors of the intervention and independent risk factors for the outcome. Brookhart et al. (2006) found that the inclusion of variables related to the outcome decreases the variance of an estimated treatment effect without increasing the bias. In

contrast, the inclusion of variables related to the treatment but not to the outcome, increases the variance of the estimated treatment effect without decreasing the bias. In the TARGET study, the inclusion of sex, age, time since transplant and presence of diabetes to eGFR, did not appear to influence the intervention effect as compared to the alternate propensity matched models. A reduction in variables to eGFR alone or eGFR, sex and age resulted in an unequal distribution of the co-variates of sex and primary etiology of ESRD. The eGFR is directly related to the intervention, or propensity to receive 'treatment' in the TARGET study, as the inclusion criteria was based on an eGFR value. The progression or change of eGFR over the 12 months is related to the outcomes, as it is known the progression of CKD stage results in a deterioration of many of the clinical targets in CKD. The association of age and sex to the progression of CKD in the kidney transplant population is not known.

The change of eGFR over time may be a more accurate variable to include in the propensity-model, as opposed to one prevalent value. The progression of kidney graft dysfunction may in part, be more closely related to both intervention and outcomes in the kidney transplant CKD population. The addition of more variables to the propensity model is likely to reduce the sample size, with the associated risk of a type two error or the failure to detect a statistically significant difference that really exists. Despite the addition of variables considered predictors of intervention and risk factors for the outcomes, there were no differences in the statistically significant outcomes between the two groups. A partial explanation may be the recognition that calculating eGFR with the MDRD formulae includes the variables of age, sex and nationality. As such, the variables of age and sex may not require a second entry into the propensity-model.

When choosing the co-variates to enter into the propensity model, it is important to know which variables influence treatment and outcome. Further studies with the kidney transplant CKD

population, should consider the use of a propensity-score method for matching if a randomized trial is not feasible. There is not sufficient data to suggest that only the co-variate of eGFR be used, therefore further study using and comparing the three propensity-score models with a larger sample size is recommended.

Adherence enhancing behaviour. One objective of this study was to determine whether there was an association between the number of patients reporting non-adherence, as measured by non-prescribed medication self-adjustment documentations, and achievement of standardized clinical targets. The medication adherence interventions consisted of specific questions related to medication taking behaviour, use of behaviour change techniques (i.e., self-efficacy enhancing strategies), medication reviews with a nephrology pharmacist, case management by the APN, and a collaborative care approach between the healthcare professionals and patients.

Surprisingly, the proportion of patients achieving the clinical targets did not differ between those who had no documented, non-prescribed medication adjustments as compared to those who had one or more documentations reflecting patient self-reported, adjustment of their medication and achievement of clinical targets. There are at least three possible explanations for the lack of statistical significance in the TARGET study findings. First, the lack of significance may be explained by the small sample size. Dichotomizing the adherence measure was based on the assumption that adherers and non-adheres are potentially distinctly different groups of individuals for determinants or predictors of adherence (i.e., characteristics of medication regimen, socio-demographic characteristics, psychosocial characteristics, social support and social environment) (Christenson, 2004). In this situation, the dichotomized measure more appropriately represented those two groups however, resulted in a reduced sample size. The resulting sample size (18 with no documentations and 43 with one or more documentations) was underpowered to detect a

significant difference. Of the patients with no documentations, 15 (83%) achieved the target score as compared to 25 (52%) with one or more documentations. This corresponds to a standardized difference of .70. Based on this difference, the study had only approximately 50% power to detect a difference of this size using the cut-off for statistical significance of 0.05. A sample size of 42 in each group would have been required to detect a significant difference at a power of .80.

Second, while the documentation of patients' reported medication adjustment was the surrogate for adherence behaviour, it is not a direct measure of a patient's adherence to medications. The patients' self-report was chosen because it is considered uncomplicated, inexpensive and feasible in most clinical settings (Schäfer-Keller et al., 2008). In addition, self-report is considered a more valid measure of adherence, as compared to electronic monitoring, particularly for the detection of missed doses and erratic timing of medication administration (Butler et al., 2004). It is, however, prone to problems of recall, the honesty of replies, and the interviewer's correct interpretation of responses (Farmer, 1999; Hansen et al., 2007).

No gold standard exists for the measurement of medication non-adherence, although researchers suggest that electronic monitoring provides a more sensitive measure of medication non-adherence (Christenson, 2004; Farmer, 1999). Any quantitative measure of medication adherence (e.g., pill counts and electronic monitoring), moreover, fails to assess the reasons why patients are non-adherent with their medications. In the kidney transplant CKD population, the most realistic measures for the practice environment may continue to be self-report in combination with serum levels of immunosuppressant agents and prescription refill records. Given the limitations of the currently available measures of non-adherence, it is important for future transplant researchers and healthcare professionals to consider the use of multiple indicators of non-adherence to minimize the impact of these limitations.

Finally, chart audit findings were used to identify the documentation of a non-prescribed, patient reported medication self-adjustment. There are inherent limitations associated with chart audits, which may influence the accuracy of the chart audit. These limitations include missing or inaccurate data, a chart auditor's lack of clinical background when making decisions regarding chart information, and incomplete documentation by the healthcare professional, even though an interaction occurred (Allison et al., 2000; Wu & Ashton, 1997).

Adherence measures and the clinical relevance. An interesting and clinically important finding in this study was that 43 (71%) of intervention patients reported one or more medication non-adherent behaviour events. This is clinically relevant because it directly relates to the transplant patient's associated risk of kidney graft failure when non-adherent to their immunosuppressant medication (De Geest et al., 1995; De Geest, Dobbels, Fluri, Paris, & Troosters, 2005). The findings of a systematic review of adherence to immunosuppressant therapy (IST) after kidney transplant indicated that the odds of graft failure increased 8%, from 4 to 12%, in patients who missed, stopped or altered their dose of IST without a physician prescription, as compared to those who made no adjustments (Butler, Roderick, Mulee, Mason, & Peveler, 2004b). It should be noted that the definitions of adherence varied across studies, and differed from the definition of adherence in the TARGET study. In much of the adherence research, the measures of non-adherence varied from study to study which limits our ability to make any specific conclusions regarding the predictive value of the number of missed or altered doses and the associated incidence of kidney graft failure. A patient's non-prescribed self-adjustment of IST accounts for up to 36% of chronic kidney graft failure among the transplant CKD population (Butler et al., 2004b; De Geest et al., 1995; Didlake et al., 1988; Nevins & Matas, 2004).

In summary, recognizing and discussing medication adherence behaviour with kidney transplant patients is an important component of patient disease self-management. When looked at in terms of the potential clinical relevance, when healthcare professionals directly questioned a patient about their medication adherence behaviour, 70% of the intervention patients in the TARGET study reported some degree of medication non-adherence. The typical adherence rates for prescribed medications across acute and chronic disease states is 50% (Haynes et al., 2005), with the kidney transplant patients' mean non-adherence rate estimated to be 22%, ranging from five to 68% (Butler et al., 2004b; Chisholm, 2002; 2004). The TARGET study is the first study to measure documentation of a patient's reported medication non-adherence, as a surrogate of non-adherence, in a population of stage 4 and 5 kidney transplant CKD patients. Given that studies suggest 36% of chronic kidney graft failure is associated with non-adherence to IST, it is interesting that when directly questioned 70% of kidney transplant CKD patients reported medication non-adherence. Comparison of the TARGET study results to those reported in the literature is limited due to the variety of non-adherence measures used in the studies. Further studies to assess the validity of the surrogate or indirect measure of a patient's medication adherence based on a healthcare professionals documentation of a patients report of missing, altering or changing of medications is required.

Measuring the dose of chronic disease management. A unique aspect of the TARGET study was the measurement of the chronic disease management intervention dose. These interventions are behavioural in nature and reflect an interaction between the healthcare professional and patient. The method for converting a behavioural intervention to an objective dose measurement is not standardized and little empirical work has been done to guide researchers or clinicians in determining the correct dose (Huber, Hall, & Vaughn, 2001; Lindsay, 2004; Reed et al., 2007).

There is consensus, however, on what the measurement of an intervention dose should contain. Similar to the concept of a medication dose, a behavioural intervention dose can be defined by the amount, frequency and duration (Huber et al., 2001; Reed et al., 2007). Amount and frequency describe how much effort is needed for the intervention, with duration being the length of time over which the intervention occurs (Huber et al., 2001).

In this study, the characteristics of the CKD focused interventions for patients were delineated, based on the Chronic Care Model. These characteristics or elements were then organized into the process measures for chronic disease management (i.e., disease self-management, shared decision-making, adherence-enhancing interventions, and community referral/resources). The number of documented interactions between the healthcare professional and patient that included these characteristics were used to calculate the amount and frequency for the intervention dose measurement. The largest dose of chronic disease management intervention, referred to as the intervention user rate (IUR), was provided by the APN. One explanation for this is the APN has broadened scope of practice and the case management component of the APN's role.

The APN role includes dimensions not necessarily within the scope of practice for other healthcare professional roles, which may increase the number and type of APN interventions and interactions with the patients. The APN scope of practice in the kidney transplant CKD clinic included providing (a) continuity of care through case management, (b) a holistic health assessment, (c) diagnosis of health problems, (d) treatment prescriptions, (e) CKD symptom screening and monitoring, (f) advocating for and referring to support services such as rehabilitation as required, and (g) the initiation of discussions on end-stage renal disease options with patients. Huber et al. (2001) uses the term 'breadth' to describe additional elements of an intervention dose. Breadth is the number and type of possible broader intervention activities specific to the actions

associated with a tailored intervention. In the APN role, these tailored intervention activities make up the breadth of the APN scope of practice and expertise.

Calculating the dose provided the opportunity to measure the healthcare professional and patient interactions focused on CDM using readily available data. The study results did not show any relationship to the outcomes, which may in part be explained by the limitations associated with chart audits and variation in healthcare professionals narrative documentation standards. In this study, despite the emphasis on CDM, healthcare professionals did not receive any special training or guidance on documentation of their CDM interactions with patients. Many healthcare professionals use a problem oriented charting methodology, which may limit documentation of content related to a fuller description of the chronic disease management interventions. Educating healthcare professionals on a standardized approach to documentation of chronic disease management interventions may improve clarity of the documentation, thereby also improving the accuracy of the intervention dose.

In terms of the association of the intervention dose or intervention user rate to the patients target achievement, there was a significantly greater mean intervention dose (3.91+/-1.46 versus 2.15 +/-0.53, $p<0.0001$) for those intervention patients who participated in end-stage renal disease options discussions as compared to those who did not participate in these discussions. The calculation for the intervention dose includes the discussions on end-stage renal disease options in addition to all chronic disease management focused discussions, which may in part explain the resulting association. The APN initiated 87% of these discussions. Detailing the breadth of the APN role in relation to the measurement of the intervention dose adds to the body of empirical research that is needed to improve the understanding and knowledge around operationalizing the measurement of

the dosage of a nursing intervention. The formulae used to calculate the intervention user rate, however, does require further testing and validation.

Study Limitations

A number of methodological limitations are relevant to this study. The method used was a non-randomized retrospective controlled study, which may introduce selection bias due to the lack of randomization. To offset this limitation, a propensity-score analysis was undertaken to account for potential confounding factors and selection biases because of the non-random allocation of the two groups. There are limitations associated with using propensity-score matching and relate to the variables not chosen to enter in to the matching analysis. Matching does not eliminate potential bias associated with unmeasured variables that may have an influence on the patient's propensity to be allocated to the treatment or the control group (Austin, 2007). Moreover, due to the small sample size for this study, there were limitations on the number of observed co-variates that could be included in the propensity score model.

Each additional variable included has the potential to reduce the sample size by eliminating further unmatched cases, thereby affecting the power required to detect a statistically significant difference between the intervention and control groups. This was found to be the case in the TARGET study. Matching on eGFR alone or eGFR, age and sex resulted in a total sample size 88. The addition of the variables diabetes, and donor type reduced the sample size to 80. However, the variables chosen for this study were based on those suggested to most influence development of CKD, influence the progression of kidney transplant CKD, and thereby reflect a propensity to intervention in the kidney transplant CKD clinic (Gill et al., 2002; Karthikeyan et al., 2003; Marcén et al., 2005).

A second methodological limitation relates to the retrospective chart audit process for data collection. No universally accepted criteria exist for a well-conducted chart audit process (Panacek, 2007). The research assistants were experienced in methods of data extraction and chart review. However, errors were identified during the verification process. All errors were corrected and reviewed with the assistants in an effort to improve accuracy, and in every fifth chart audit, the case report form data was verified with the source documents. Despite use of these methods to increase the accuracy and reliability of the data collection, a potential risk for human error remains.

A further limitation, in terms of internal validity, is the potential for effects of co-intervention on the study outcomes. Patients in the intervention and control groups may have accessed information or support in addition to that provided during the clinic visit that could in turn influence the achievement of clinical targets. Although, considering the similarity of the clinic environment for both groups, there is no reason to believe the access to additional information or support was different between the two groups. A limitation to the study's external validity may be attributed to experimenter and study effects. The National Kidney Foundation introduced new guidelines for the care of kidney transplant and CKD patients in 2004 and 2006, which may have increased the healthcare professional's attentiveness and documentation related to the implementation of treatment standards for the management of CKD. The increased attentiveness may also have resulted from the healthcare professional's involvement in the initial implementation of the APN kidney transplant CKD clinic. There was some potential for bias related to the researcher also being the clinic APN in this APN led clinic. A number of strategies were used to minimize the potential for this to influence the study results, which included (a) external research assistants for the chart audits and data extraction, (b) external statistician for all

data analysis, and (c) propensity-score matching that resulted in blinding of the matched pairs to the researcher.

Research and Practice

This study has provided a solid foundation for larger scale evaluations of an APN led inter-professional collaborative chronic care approach for kidney transplant CKD patients. The study results not only add to the body of evidence in support of the APN role for improving patient outcomes in chronic disease, it is in keeping with the Canadian Nurses Association (2008) recommendations for evaluating the implementation of a new APN role.

Future nursing research. A number of future nursing research opportunities have been highlighted in the above discussions. These include (a) further chronic disease management intervention studies focusing on the individual influence of certain components to patient outcomes (e.g., APN collaborative practice, shared decision-making, and clinician decision support), (b) combined measures of medication non-adherence, and (c) full cost-benefit analysis of the value-added component of the APN role. There is also a need to improve nursing knowledge and measurement of the dose-response relationship using a more objective approach to support decisions about what interventions nurses should use and how much (Reed et al., 2007). In a review of 47 controlled clinical trials of nursing interventions, published between 2000 and 2001, none were found to provide sufficient information on dose (Lindsay, 2004). It is recommended that future research measuring the effectiveness of a nursing intervention include an explicit description of the intervention dose as was attempted to do in the TARGET study (Brooten & Youngblut, 2006). The measurement of the APN and inter-professional team CDM intervention dose requires further validation and may offer a practical method for nursing researchers to deal with the difficult issues in operationalizing the dosage of a nursing intervention.

Support of patient decision-making is a further area of potential nursing research. In the TARGET study, intervention patients participated in more discussions on end-stage renal disease options as compared to the control group. These discussions represent nursing practice opportunities for engaging patients in questions around their decisional conflict associated with these choices. The recent best practice guideline on decision support for adults living with CKD, developed with RNAO (Bruner et al., 2009), can be used by nurses caring for kidney transplant CKD patients, who face many of the same decisions. The decision related to a second kidney transplant, repeated exposure to high-dose immunosuppressant medication with the second transplant and return to dialysis are unique to the transplant CKD population. Moreover, due to the slower progression of CKD in the kidney transplant population (Djamali et al., 2003), patients accommodate and fail to recognize the progression of the associated uremic symptoms, as is the case in many chronic disease conditions (WHO, 2002). This makes it more difficult for nurses to engage patients in discussions around end-stage renal disease options or identify areas of decisional conflict. To determine the quality of these decision support discussions, instruments such as the Decision Support Analysis Tool (DSAT-12) could be used to provide feedback to the APN (Stacey, Taljaard, Drake, & O'Connor, 2008).

There is an ongoing debate among nephrology healthcare clinicians regarding the optimal time for discussing and initiating end-stage renal disease options with patients; most of the debate revolves around the non-transplant CKD population (Arora et al., 1999; Levin et al., 2008; Mendelssohn et al., 1999). Healthcare clinicians often initiate these discussions based on a gestalt assessment, which includes (a) the patient's rate of kidney failure, (b) the presence of, or increase in, proteinuria, (c) the progression of a patient's uremic symptoms (i.e., nausea/emesis, fatigue, muscle discomfort, edema, sleep disturbance, loss of appetite, weight loss), and (d) the progression

of metabolic markers (i.e., creatinine, eGFR, urea, acidosis, anemia). The patients readiness to engage in these conversations and their understanding of the risks associated with a delay in dialysis or re-transplant, are significant factors influencing nurses ability to support the patients' decision-making processes. The implementation and evaluation of the RNAO CKD best practice guideline (Bruner et al., 2009) for the transplant CKD population may provide nurse's with the tools shown to be effective in identifying the decisional conflict associated with the options of a return to dialysis, repeat kidney transplant from a living or deceased donor, or palliation.

Few nursing studies have taken the novel approach of using the propensity-score method to address the lack of randomization (Qin, Titler, Shever, & Kim, 2008). Results of the TARGET study provide evidence of the effectiveness of propensity-score matching to balance co-variates between the control and intervention groups in a non-randomized trial. The decision criteria for choosing the best propensity-score model does require future research to address the gap in understanding the association between the TARGET studies three propensity models differing co-variate balance, yet similar results.

Recommendations for future nursing practice. The key recommendation for future nursing practice is sustaining and expanding the APN collaborative practice role in the management of patients with kidney transplant CKD. The sustainability of evidence-based practice innovations, such as this APN-led transplant CKD clinic, requires organizational support, leadership, health professional resources and ongoing evaluation of its influence on health care outcomes (Davies, Tremblay, & Edwards, 2010). The TARGET study intervention outlined the case management and collaborative practice components of the APN role, based on the principles of the CCM. Advanced nursing practice is what an APN does within the expanded role (Bryant-Lukosius et al., 2004). Developing competency in the integration of case management skills and collaborative

practice reflect how the APN role continues to evolve, requiring new knowledge and expertise for select patient populations. The implementation of APN roles requires the identification of a service need or practice gap and is a significant factor in determining the success of the role (DiCenso & Bryant-Lukosius, 2010). The contribution of the APN role in chronic disease management for kidney transplant CKD patients provided evidence of a successful collaborative practice environment and further expansion of the role to guide development and evaluation of future APN led approaches to health care.

Implications for Future Policy

The primary policy implication for this study relates to advocating for sufficient resources and infrastructure for APN led collaborative practice clinics for patients with chronic disease. DiCenso and Bryant-Lukosius in a recent decision support synthesis, recommended "APN positions and funding support should be protected following implementation and demonstration initiatives to ensure some stability and sustainability for these roles once they have been incorporated into the healthcare delivery system." (DiCenso & Bryant-Lukosius, 2010, p 51). The support must come from many levels, including leadership by the Canadian Nurses Association, other nursing and local healthcare organizations and governments, to encourage creation of APN roles aligned with the changing health of our population (CNA, 2009).

The end-stage renal disease patient population is rapidly growing in sharp contrast to the declining number of nephrology experts (Kletke, 1997; Zimmerman, Selick, Singh, & Mendelssohn, 2003). For example, in Canada it is increasing at 9% per year with an associated increase in the ratio of dialysis patients per nephrologist (CIHI, 2006). Current nephrology human resources will become increasingly insufficient to provide optimum care for dialysis and transplant patients in the traditional manner (Zimmerman et al., 2003). The demand for APN roles has

increased as a strategy to develop sustainable models of healthcare (Bryant-Lukosius et al., 2004). Healthcare policy must keep pace with formalizing the legislation and regulation for the full integration of APN's. The key policy priorities include (a) standardizing APN regulatory and educational requirements, (b) promoting awareness of the role, and (c) protecting funding support for APN positions (DiCenso & Bryant-Lukosius, 2010).

Conclusion

In summary, the TARGET study is the first to evaluate the implementation of an APN led inter-professional collaborative chronic care approach using a structure and process analysis for enhancement of outcomes in kidney transplant CKD patients. The evaluation showed that patients exposed to the APN led clinic (a) are more likely to attain the targeted clinical outcomes and participate in discussions about ESRD options, (b) have fewer hospital admissions and emergency department visits; and (c) are more likely to have K/DOQI standards implemented in their care. A substantial amount of other research has been focused on the association between individual components or interventions based on the CCM and patient outcomes (Adams et al., 2007; Bodenheimer et al., 2002; Glasgow et al., 2001; Litaker et al., 2003; Watts et al., 1995; 2009).

Wagner's (1998) original intent in developing the CCM, however, was to provide a multi-dimensional framework, which highlighted for healthcare professionals where and how to best manage and support the long-term management of patients with complex, chronic health care needs. It was not the intent of the TARGET study to identify the one component that most influenced the patient outcomes. The reality, in the majority of health care settings, is that no one healthcare professional or intervention can be given credit for improving or optimizing the quality of health care. It is, more often than not, the collaborative effort and influence of many healthcare professionals, interventions, and technologies. As the first study of an alternate approach to the

health care specific to the kidney transplant CKD population, these results provide the foundation for future research, across multiple kidney transplant programs to further the evidence in support of a chronic care approach to improve outcomes for kidney transplant patients with CKD.

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Appendix I

Studies Evaluating Effectiveness of Advanced Practice Nurse (APN) Approaches for Chronic Health Care

Author	Purpose	Design/Sample/Setting	Methods/Intervention	Results
Allen et al., 2002	Effectiveness of a post-discharge APN-care management (CM) model for stroke and transient ischemic attack (TIA).	Randomized controlled trial (RCT). N= 93 Post stroke or TIA patients, 48 hours prior to discharge randomized to receive APN-CM (n=47) or usual post-discharge care by their primary care physician (PCP) (n=46).	**Intervention:** APN-CM telephone assessment 3 to 7 days post-discharge. Within 1 month post discharge, APN-CM home visit, standardized bio-psychosocial assessment for specific post stroke problems. Within 7 days of home visit, APN-CM consultation with post stroke team to discuss findings. Treatment plan implemented by APN-CM in collaboration with patients PCP. **Control:** Post-discharge care by PCP.	A positive effect size across the 5 domains of neuromotor function, severe complications, quality of life, management of risk, and stroke knowledge. Largest effect size with stroke knowledge (.98, CI .59, 1.4), smallest for neuromotor function (.10, CI -.29, .50). Global significance test based on ranks remained significant ($p<0.0001$).
Callahan et al., 2006	Effectiveness of an APN collaborative practice model to improve the quality of care for older adults with Alzheimer disease.	RCT N=153 Older adults with Alzheimer's randomized to collaborative practice (n=84) or augmented usual care (n=69) in a primary care setting.	**Intervention:** 1 year of care management by an interdisciplinary team led by an APN in collaboration with PCP. APN served as case/care manager. Use of standard protocols to initiate treatment. **Control:** Care managed by PCP, pursued any evaluation or treatment they deemed appropriate	89% of intervention patients triggered at least 1 protocol for behavioural and psychological symptoms of dementia. Intervention patients more likely to receive cholinesterase inhibitors (79.8% vs 27.5%; $p=0.03$); significantly fewer behavioural/psychological symptoms of dementia (Neuropsychiatric Inventory score, mean difference -5.4, $p=0.01$). No differences on cognition, activities of daily living, rates of hospitalization, nursing home placement or death.
Cowan et al., 2006	To compare NP/PCP collaborative management of hospital care, expedited discharge, and follow-up to usual management.	Comparative, 2-group quasi-experimental design. N=1207 General medicine inpatients receiving NP/PCP care (n=581) versus usual care (n=626).	**Intervention:** APN, hospitalist and multidisciplinary team managed patient care during hospitalization. Daily rounds. APN follow-up phone call up to 30 days after discharge. **Control:** Usual care management which did not include APN. Weekly rounds.	Length of stay significantly lower in treatment group (5+/- 6.3 versus 6.01 +/- 6.9 days, $p=0.0001$). Cost savings US$1707 per day for one day of earlier discharge. No significant difference between groups in readmission rates or mortality within the first 4 months after discharge.

Studies Evaluating Effectiveness of Advanced Practice Nurse (APN) Approaches for Chronic Health Care (continued)

Author	Purpose	Design/Sample/Setting	Methods/Intervention	Results
Felber-Neff, D., et al., 2003	Examined the use of an APN transitional model for home care patients with Chronic Obstructive Pulmonary Disease (COPD).	Prospective quasi-experimental study. N=80 APN-directed team caring for out patients with COPD (n=41) versus RN providing routine home care to control group (n=39).	**Intervention:** APN-directed/supervised pulmonary disease management group. APN care included home visits, telephone contact, clinical consultation for patients identified as high risk, home visits for teaching, assessment of complex care needs. **Control:** Primary nursing care by RN or LPN with generalized skills. Care included assessment of patients', physical, psychological, environmental and social support needs.	Intervention group reduction in health service use, re-hospitalization and acute care visits ($p<.05$). Control patients significantly more depressive feelings ($p<.05$) and poorer ADL status ($p<.05$). No group differences for instrumental activities of daily living (IADL) or dyspnea.
Graham et al., 2006	To evaluate the impact of collaborative practice teams with a NP and PCP on quality of process-of-care, self-care and proxy measures for health outcomes for patients with diabetes and HTN.	Pre-post intervention audit at four participating sites. N=752 Sampling population derived from four primary care sites in Nova Scotia. Electronic and chart audits completed for n=211 patients with diabetes, n=541 with HTN.	**Intervention:** Collaborative practice teams included NP and PCP. Information systems at each site included practice and clinical management components. Information systems did not include any specific electronic support mechanisms or triggers for clinical management of diabetes or HTN. **Control:** not applicable	**Diabetes Care**: 1.82 times more likely to achieve BP target (OR 1.82, CI .98- 3.5, $p<0.05$), 2.05 times more likely to be screened for nephropathy ($p<0.001$), 1.6 times more likely to be screened for retinopathy ($p<0.05$). Home glucose monitoring increased by 7.6% (OR 2.2, CI 1.16-4.36, $p<0.001$). No difference in educational components. **HTN Care:** 2.73 times more likely to achieve SBP < 140 (OR 2.73, CI 1.93-3.94, $p<0.001$), 2.24 times more likely to achieve DPB < 90 (OR 2.24, CI 1.47-3.49, $p<0.001$). Lipid profile monitoring increased by 6.5 % (OR 1.53, CI 1.11-2.23, $p<0.05$).Lifestyle modification measures no change, except for routine assessment of weight (OR 7.86, CI 3.57-20.45, $p<0.001$) and exercise counselling (OR 2.48, CI 1.62-3.90, $p<0.001$).

Studies Evaluating Effectiveness of Advanced Practice Nurse (APN) Approaches for Chronic Health Care (continued)

Author	Purpose	Design/Sample/Setting	Methods/Intervention	Results
Harwood et al., 2004	Does NP/CNS-Nephrologist collaborative practice versus Nephrologist only influence in-centre hemodialysis patient outcomes?	Retrospective cross-sectional study. N= 112 Groups stratified based on care by Nephrologist (n=29) versus NP/CNS in collaborative care with Nephrologist (n=83).	**Intervention**: NP/CNS –Nephrologist collaborative practice for hemodialysis patients during day shift. Use of medical directives to support NP/CNS clinical decision making. **Control:** Evening shift of hemodialysis patients under care of Nephrologist only.	Team satisfaction and perceptions of care delivery higher in NP/CNS nephrologist group ($p<0.0001$). More adjustments made to target weights ($p<0.004$) and medications by NP/CNS nephrologist group ($p<0.004$). No differences for emergency visits, admissions to hospital and length of stay.
Lee et al., 2007	Effectiveness of a chronic kidney disease (CKD) clinic led by APN-NP in achieving National Kidney Foundation Kidney Disease Outcomes Quality Initiative (K/DOQI) targets.	Retrospective chart review. N= 113 Data collected and compared for (n=77) patients in CKD clinic and (n=36) patients from renal-hypertension (HTN) clinic at initiation of dialysis and 12 months post initiation of dialysis.	**Intervention:** Patients in CKD clinic cared for by trained renal APN/NP who followed protocols based on K/DOQI guidelines in collaboration with nephrologist. **Control:** Patients in renal-HTN clinic cared for by nephrologists in training under supervision of board certified nephrologists.	CKD patients higher haemoglobin ($p=0.02$), albumin ($p=.002$), darbepoetin replacement therapy ($p=0.009$), phosphate binders ($p=0.01$), dietary counselling ($p<0.0001$) and dialysis education ($p<0.0001$). Higher percentage of CKD patients had functioning permanent vascular access at start of dialysis ($p<0.0001$). Renal-HTN patients greater decline in DBP ($p=0.04$), haemoglobin ($p=.009$), albumin ($p=0.005$), and more all cause hospitalizations (86.1 % versus 50.6%, $p<0.0001$).
Litaker et al., 2003	Comparing a traditional physician only model of care to NP-physician team based approach to chronic disease management.	RCT N=157 Patients with mild or moderate hypertension and non-insulin dependent diabetes randomized to either NP-MD team (n=79) or usual primary care physician (n=78).	**Intervention:** Main components focused on chronic disease management and use of clinical practice algorithms, patient education on disease self-management strategies, regular monitoring and feedback delivered primarily by the NP. **Control:** Physician only, or usual care defined as any form of treatment offered by an individual's PCP.	NP-MD team patients improvement in diabetes control (HbA1C mean change -0.63, $p= .02$), change of patient satisfaction from baseline (+6.2 vs -1.7, $p=0.01$) and documented counselling for life style change ($p<0.001$). NP-MD team average patient contact time 180 mins versus 85 mins for usual care patient. ($p<0.001$). No significant differences in achieving nationally recognized treatment goals for blood pressure or total cholesterol.

Studies Evaluating Effectiveness of Advanced Practice Nurse (APN) Approaches for Chronic Health Care (continued)

Author	Purpose	Design/Sample/Setting	Methods/Intervention	Results
Naylor et al., 2004	To examine the effectiveness of a transitional care intervention delivered by APN's to elders hospitalized with heart failure.	RCT N=239 Six academic and community hospital settings, study included hospitalized elders, aged 65 and older with heart failure. Intervention patients (n=118) with APN directed discharge compared to usual discharge planning (n=121).	**Intervention:** A three-month APN directed discharge planning and home follow-up protocol. **Control:** Usual care	Time to readmission or death longer in intervention group (p=.026), at 52 weeks fewer readmissions (105 vs 162, p=0.047) and lower mean total costs (US$7,636. vs US$12,481., p=0.002), short-term improvement in overall quality of life at 12 weeks (p<0.05). No significant difference between groups in functional status.
Naylor et al., 1999	Do vulnerable elders with heart failure experience improved outcomes when APN's coordinate care in the transition from hospital to home?	RCT N= 262 Two urban, academically affiliated hospitals, study included hospitalized elders at risk for re-admission. Intervention patients (n=124) received comprehensive discharge planning versus usual care (n=138).	**Intervention**: APN protocol directed care: daily hospital visit, collaborate with healthcare team, patient visit 24hrs post discharge, weekly in first month, bimonthly next 2 months, patient and caregiver telephone access to APN. **Control:** Usual care.	Significantly reduced re-hospitalizations related to co-morbid conditions in intervention group (p<0.013). Time to re-admission increased in intervention group (p<0.001) No significant difference in post discharge acute care visits, functional status, depression or patient satisfaction.

Studies Evaluating Effectiveness of Advanced Practice Nurse (APN) Approaches for Chronic Health Care (continued)

Author	Purpose	Design/Sample/Setting	Methods/Intervention	Results
Vrijhoef et al., 2001	To assess patient outcomes, when care for outpatients with stable type 2 diabetes is transferred from internist to nurse specialist.	A 12 month non-equivalent control group design. General |Practitioners referred diabetes patients to the traditional model (n=47) or nurse specialist model (n=52).	**Intervention:** Patients receive 3 quarterly consultation visits with nurse specialist. Annual consultation/assessment with internist. Protocol driven care. **Control:** Patient receives quarterly consultations/assessments with internist.	Glycemic control improved for intervention patients (8.6% to 8.3%, *p*=.001) and deteriorated in control patients (8.6% to 8.8%, *p*=.001). Equivalent outcomes achieved for lipid levels, BP, and weight.
Wong et al., 2005	To compare outcomes of diabetic patient undergoing early discharge and follow-up by APN/Nurse Specialist or routine care.	RCT N=101 Candidates needing to remain in hospital for glycemic control randomized to early discharge/APN follow-up group (n=52) or routine diabetic care in hospital (n=49).	**Intervention:** APN/Diabetes Nurse specialist taught essential self-care skills and reviewed prior to discharge. APN phoned patient every 1- 2 weeks until glycemic levels stable, in addition to monitoring health behaviours, medication taking and checking of glucose level. APN adjusted medications according to glycemic levels. Return appointment at 12 and 24 weeks for both groups. **Control:** Patients remained in hospital until glycemic level stable, discharged based on attending physician recommendation. Diabetes education during hospitalization by diabetes nurse.	Treatment group had significant improvement or higher result for blood glucose monitoring ($p<0.001$), exercise adherence ($p<0.001$). Length of hospital stay (LOS) significantly different, mean difference LOS 3.7 days ($p<0.001$). Better improvement in HbA1c with treatment group (7.6% vs 8.1%, $p=0.06$) No significant difference between the groups for medication adherence, body weight, and frequency of hospital readmission.

Appendix II

The Target Study Patient Case Report Form

Patient Number: ☐☐☐ Date: dd☐☐ mm☐☐/yyyy ☐☐☐☐ Grp R☐ P☐

INCLUSION CRITERIA (To be eligible for the study the answer must be "yes" to the following questions):

1. Patient attended the Ottawa Hospital renal transplant clinic during the study period.
2. One or more years since kidney transplantation.
3. CKD classification of Stage 3 or lower, eGFR ≤ 60 mL/min/1.73 m² for 3 months or greater, measured using the abbreviate Modification of Diet in Renal Disease (MDRD)

EXCLUSION CRITERIA (To be eligible for the study the answer must be "no" to the following questions):

YES NO

1. A clinical diagnosis of acute kidney graft rejection.
2. Undergoing active treatment or investigation for malignancy.

PATIENT DEMOGRAPHICS

Date of Birth: mm☐☐/vvvv☐☐☐☐ **Sex**: 1 ☐ Male 2 ☐ Female

Race: 1 ☐Caucasian/White **2**☐Black **3** ☐Aboriginal **4** ☐Asian **5** ☐Latin American

Primary Etiology of Renal Disease:

☐ **1** Diabetes mellitus ☐ **2** Polycystic kidney disease ☐ **3** Hypertension

☐ **4** Interstitial Nephritis ☐ **5** Obstructive/Reflux ☐ **6** Unknown ☐ **7** Glomerulonephritis

☐ **8** Lupus ☐ **9** Drug induced ☐ **10** Vasculitis ☐ **11** Renal Dysplasia ☐ **12** Other _____

Date of current Transplant: dd☐☐/mm☐☐/yyyy☐☐☐☐

Primary Transplant:1☐ **Yes** 2 ☐ > 1 transplant **Donor: 0** ☐ Deceased **1** ☐ living

Date of previous Transplant: dd☐☐/mm☐☐/yyyy☐☐☐☐

Patient Number: ☐☐☐ **Baseline Variables** Date: dd☐☐/mm☐☐/yyyy☐☐☐☐			Achieved target
Variable **Creatinine 1. 2. 3.** **mean_____ eGFR _____ mdn_____ eGFR_____**	**Value** **Mn**	**Md**	**YES(1) NO(2)**
1. Blood Pressure (average of 3 most recent BP) *Systolic BP≤ 130 and Diastolic BP ≤ 80* 1. 2. 3.			○ ○
2. Hemoglobin *105-120 g/L (≥100 if not on aranesp)* *1. 2. 3.*			○ ○
3. Lipids *LDL ≤ 2.6* *1. 2. 3.*			○ ○
4. Parathyroid hormone level *< 33.0 pmol/L (normal to < 2 x upper normal)* *if parathyroidectomy(N/A)*	n/a	n/a	○ ○
5. Calcium *2.25 – 2.45 mmol/L* • after adjusting for serum albumin using standard correction factors 0.02 mmol/L for every 10 units of albumin lower than 40 *1. 2. 3.*			○ ○
6. Phosphate *0.6 - 1.8 mmol/L* *1. 2. 3.*			○ ○
7. Carbon dioxide (Co2) *22-27 mmol/L* *1. 2. 3.*			○ ○
8. Presence of functional dialysis access prior to study start date: **circle type if yes fistula/graft peritoneal catheter permcath**			○ ○
Other Co-morbid conditions:			
			YES(1) NO(2)
Current smoker Unknown ☐			○ ○
Myocardial Infarct / Angina (Coronary Art Disease-CAD)			○ ○
Hypertension (Cardiovascular disease - CVD)			○ ○
Congestive Heart Failure			○ ○
Peripheral vascular disease (PVD)			○ ○
History of cancer			○ ○
Other (please specify):			
Current Immunosuppressant Medications: Baseline			**YES(1) NO(2)**
Tacrolimus (Prograf) – FK			○ ○
Cyclosporin (Neoral)			○ ○
Sirolimus (Rapamune)			○ ○
Mycophenolate Mofetil (Cellcept)- MMF			○ ○
Mycophenolate Sodium (Myfortic)			○ ○
Prednisone			○ ○
Azathioprine (Imuran)			○ ○

Patient Number: ☐☐☐ **Current Medication Regime : Baseline**	
Anti-Hypertensives (write name of medication)	**YES(1) NO(2)**
Beta-Blocker: metoprolol/atenolol/propranolol/pindolol/bisoprolol	○ ○
ACE-Inhibitor: ramipril(altace)/ perindopril(coversyl)/captopril (capoten)/enalapril(vasotec)	○ ○
Angiotensin Receptor Blocker: Cozaar (losartan), Avapro(irbesartan), Diovan (valsartan), Micardis (telmisartan)	○ ○
Alpha Andrenergic Antagonist: clonidine (catapres)/minipress(prozosin)/cardura (doxazosin)/hytrin (terazosin)	○ ○
Calcium Channel Antagonist: Cardiazem(diltiazem)/ verapamil(isoptin)/norvasc(amlodipine)/cardene (nicardipine)/ procardia (nifedipine)	○ ○
Vasodilator: minoxidil (loniten), hydralazine (apresonline), nitropatch	○ ○
Diuretic: lasix (furosemide/novo-semide)	○ ○
Thiazide: hydrocholorothiazide (HTCZ)/metolazone/chlorthalidone	○ ○
Other (specify):	○ ○
Lipid Lowering Agents	**YES(1) NO(2)**
Statin (specify): lipitor(atorvastatin)/pravachol(pravastatin)/Zocor(simvastatin)/mevacor(lovastatin/ lescot(fluvastatin)	○ ○
Ezitimibe(ezetrol):	○ ○
Glucose Controlling Agents	**YES(1) NO(2)**
Insulin	○ ○
Metformin(glucophage)/glyburide(diabeta)/rosiglitazone(avandia)	○ ○
Other:	○ ○
Current Medication Regime : Baseline	
Phosphate Binders/ Vitamin/Calcium/Potassium supplements	**YES(1) NO(2)**
Calcium Carbonate (Tums)	○ ○
Calcium Acetate	○ ○
Sevelamer Hydrochloride (Renagel)	○ ○
Rocaltrol	○ ○
Replavite	○ ○
Fosamax(alendronate)/Actonel	○ ○
Vitamin D	○ ○
Sodium Bicarb (baking soda)	○ ○
Potassium/K-dur/Slow K/K-lyte:	
Other (specify):	○ ○

Patient Number: ☐☐☐	
Anti-Platelet/anti-coagulant Therapy	**YES(1) NO(2)**
Acetylsalicylic acid (Aspirin-ASA)	○ ○
Clopidogrel (Plavix)	○ ○
Warfarin (Coumadin)	○ ○
Hemoglobin and Iron Supplements	**YES(1) NO(2)**
Ferrous gluconate or fumerate or sulphate	○ ○
Aranesp/EPO	○ ○
Folic Acid/Folate	○ ○
B12	○ ○
GI	
Ranitidine (zantac)	○ ○
Losec (pantoloc)	○ ○
Domperidone (motilium)	○ ○
Gravol	○ ○
Other	
Allopurinol	○ ○
Colchicine	○ ○
Eltroxin(Levothyroxine)	○ ○
Additional Medications (Specify):	

Process Outcome Measures

Process Indicators

Intervention/interaction consists of a documented encounter in which counseling; education, advice, teaching or instruction is received by the patient from the healthcare provider in the form of a discussion and/or written material. In order to qualify, the notation must include **at least one** of the following characteristics:

1. Involvement of the patient in the management of the disease (i.e., something that the patient will do, is able to do due to instruction, not something the provider will do).
   - We talked about the importance of appropriate foods and diet.
   - Can state what foods to avoid for low-salt diet
   - Advised to do daily weights
   - Encouraged to walk 5-6 days/week, will exercise more
   - Patient is reluctant to or is resistant to doing recommended risk management (e.g. resistant to beginning an exercise program, smoking cessation).
2. Written material about the disease, medication, risk factors, complications, is given to or discussed with the patient.
3. A checklist completed by provider or patient that indicates what type of counseling or advice was given to the patient or addressed at the visit (i.e., implies a discussion took place).

Patient Number: ☐☐☐ ***Total # Clinic Visits in Study Period***						Total # of Documentations
Disease Self Management						
Interaction Content Total and Healthcare Professional Involved *A=APN D= Dietitian N=Nephrologist P=Pharmacist S=Social Worker R=RN*						
1. Weight management strategies.						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
2. Nutritional management: sodium, phosphate, protein intake. *Counseling regarding diet (e.g. low salt, protein intake, fluid intake, phosphate/calcium intake, portion size, low cholesterol/fat).*						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
3. Risk factor reduction: sun protection, mosquito avoidance/protection.						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
4. Recognition and management of uremic symptoms: fatigue, nausea, decreased appetite, vomiting, difficulty sleeping, muscle cramps, weight loss.						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
5. Signs and symptoms of hypo/hyperglycemia: diaphoresis, light headed, dizzy, decreased concentration.						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
6. Cardiac disease risk reduction discussion: smoking cessation, weight management, blood pressure management, blood glucose management						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
7.. Medication adverse drug effects and alternatives. *Counseling may be regarding side effects, how to take/administer the medication.*						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
8. Home monitoring discussed - BP, weight, food portions, capillary glucose.						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
Decision Support						
Interaction Content Total and Healthcare Professional Involved *A=APN D= Dietitian N=Nephrologist P=Pharmacist S=Social Worker R=RN*						Total # of Documentations
1. Medication taking behaviour/adherence. *The note must imply or state that the patient adjusted or omitted a medication without the APN or physician prescription.*						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
2. Vaccination status and options.						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
3. Lifestyle choices: smoking status, alcohol intake, exercise level.						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	

Patient Number: ☐☐☐						
4. Advance directives. Discussion of choices related to end of life, resuscitation options, power of attorney.						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
5. ESRD options discussed including re-transplantation, vascular access, dialysis or no treatment.						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
6. Referral to ESRD options education						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
Community Resources						
Interaction Content Total and Healthcare Professional Involved *A=APN D= Dietitian N=Nephrologist P=Pharmacist S=Social Worker R=RN*						Total # of Documentations
1. Referral to weight management program.						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
2. Referral to smoking cessation program.						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
3. Referral to rehabilitation program.						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
4. Referral to diabetes education program.						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
5. Referral to psycho/social/family counselling.						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
6. Referral to financial support services.						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	
7. Referral for pain management.						
A(1) =	D(2) =	N(3) =	P(4) =	S (5)=	R(6)=	

Outcome(Study end Date) Variables Date: dd ☐☐mm☐☐/yyyy☐☐☐☐

Variable			
Creatinine 1. 2. 3. **mean_____ eGFR _____ mdn_____ GFR_____**	**Value** **Mn**	**Md**	**YES(1) NO(2)**
1. Blood Pressure (average of 3 most recent to end date) *Systolic BP≤ 130 and Diastolic BP ≤ 80* *1. 2. 3.*			○ ○
2. Hemoglobin *105-120 g/L* *1. 2. 3.*			○ ○
3. Lipids *LDL < 2.6* *1. 2. 3.*			○ ○

Patient Number: ☐☐☐			
4. Parathyroid hormone level *< 33.0 pmol/L (normal to < 2 x upper normal) - if parathyroidectomy N/A*			○ ○
5. Calcium *2.25 – 2.45 mmol/L* • after adjusting for serum albumin using standard correction factors 0.02 mmol/L for every 10 units of albumin lower than 40 • Albumin values if lower than 40 if available when Ca measured *1. Ca Alb 2 .Ca Alb 3. Ca Alb* *1. Cor Ca_____n/a 2. Cor Ca_____n/a 3. Cor Ca_____n/a*			○ ○
6. Phosphate *0.6 - 1.8 mmol/L* *1. 2. 3.*			○ ○
7. Carbon Dioxide – Co2 *22-27 mmol/L* *1. 2. 3.*			○ ○
8. End-stage renal disease options discussed • dialysis choice, re-transplant choice	**N/A**		○ ○
9. Dialysis access inserted during study period: if yes circle type fistula/graft peritoneal catheter permcath	**N/A**		○ ○

Outcome Immunosuppressant Medications:	**YES(1) NO(2)**
Tacrolimus (Prograf)	○ ○
Cyclosporin (Neoral)	○ ○
Sirolimus (Rapamune)	○ ○
Mycophenolate Mofetil (Cellcept)	○ ○
Mycophenolate Sodium (Myfortic)	○ ○
Prednisone	○ ○
Azathioprine (Imuran)	○ ○
Anti-Hypertensives (write name of medication)	**YES(1) NO(2)**
Beta-Blocker: metoprolol/atenolol/propranolol/pindolol/bisoprolol	○ ○
ACE-Inhibitor: ramipril(altace)/ perindopril(coversyl)/captopril (capoten)/enalapril(vasotec)	○ ○
Angiotensin Receptor Blocker: Cozaar (losartan), Avapro(irbesartan), Diovan (valsartan), Micardis (telmisartan)	○ ○
Alpha Andrenergic Antagonist: clonidine (catapres)/minipress(prozosin)/cardura (doxazosin)/hytrin (terazosin)	○ ○
Calcium Channel Antagonist: Cardiazem(diltiazem)/ verapamil(isoptin)/norvasc(amlodipine)/cardene (nicardipine)/ procardia (nifedipine)	○ ○
Vasodilator: minoxidil (loniten), hydralazine (apresonline), nitropatch	○ ○
Diuretic: lasix (furosemide/novo-semide)	○ ○
Thiazide: hydrocholorothiazide (HTCZ)/metolazone/chlorthalidone	○ ○

Lipid Lowering Agents **Patient Number**: ☐☐☐	○ ○
Statin (specify): lipitor(atorvastatin)/pravachol(pravastatin)/Zocor(simvastatin)/mevacor(lovastatin/ lescot(fluvastatin)	○ ○
Ezitimibe(ezetrol):	○ ○
Glucose Controlling Agents	**YES(1) NO(2)**
Insulin	○ ○
Metformin(glucophage)/glyburide(diabeta)/rosiglitazone(avandia)	○ ○
Phosphate Binders/ Vitamin/Calcium/Potassium supplements	**YES(1) NO(2)**
Calcium Carbonate (Tums)	○ ○
Calcium Acetate	○ ○
Sevelamer Hydrochloride (Renagel)	○ ○
Rocaltrol	○ ○
Replavite	○ ○
Fosamax(alendronate)/Actonel	○ ○
Vitamin D	○ ○
Sodium Bicarb (baking soda)	○ ○
Potassium/K-dur/Slow K/K-lyte:	○ ○
Anti-Platelet/anti-coagulant Therapy	○ ○
Acetylsalicylic acid (Aspirin-ASA)	○ ○
Clopidogrel (Plavix)	○ ○
Warfarin (Coumadin)	○ ○
Hemoglobin and Iron Supplements	○ ○
Ferrous gluconate or fumerate or sulphate	○ ○
Aranesp/EPO	○ ○
Folic Acid/Folate/B12	○ ○
GI	
Ranitidine (zantac)/ Losec (pantoloc)	○ ○
Domperidone (motilium)	○ ○
Other	
Allopurinol	○ ○
Colchicine	○ ○
Eltroxin(Levothyroxine)	○ ○
Additional Medications (Specify):	

Appendix III
Research Ethics Board Study Approval

The Ottawa Hospital | L'Hôpital d'Ottawa

Research Ethics Board
Conseil d'éthique en recherches

Monday, March 02, 2009

Ms. Janice Bissonnette

Dear Ms. Bissonnette:

Re: Protocol # 2009040-01H **The Target Kidney Transplant-CKD Study: Targeting Achievement of Renal Goals with Enhanced Care Teams**

Protocol approval valid until - Monday, March 01, 2010

Thank you for your letter dated January 30, 2009. I am pleased to inform you that this protocol underwent expedited review by the Ottawa Hospital Research Ethics Board (OHREB) and is approved. No changes, amendments or addenda may be made to the protocol or the consent form without the OHREB's review and approval.

Approval is for the following:
- Protocol received January 30, 2009
- Case Report Forms

If the study is to continue beyond the expiry date noted above, a Renewal Form should be submitted to the OHREB approximately six weeks prior to the current expiry date. If the study has been completed by this date, a Termination Report should be submitted.

The Ottawa Hospital Research Ethics Board is constituted in accordance with, and operates in compliance with the requirements of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans; Health Canada Good Clinical Practice: Consolidated Guideline; Part C Division 5 of the Food and Drug Regulations of Health Canada; and the provisions of the Ontario Health Information Protection Act 2004 and its applicable Regulations.

Yours sincerely,

Raphael Saginur, M.D.
Chairman
Ottawa Hospital Research Ethics Board

/cb

Appendix IV
Medical Directives

TITLE:	**Medical Directives:** The prescribing of medications, ordering of laboratory and diagnostic tests by the APN (Advanced Practice Nurse) for Renal Transplant Clinics.	NUMBER:	RTP 4.0 Med Dir 1.00
PROGRAM:	☐ CRITICAL CARE/EMERG MED ☐ TOHRCC ☒ MEDICINE ☐ HEART INSTITUTE ☐ PSYCHIATRY ☐ OBS/GYN ☐ REHABILITATION ☐ SURGERY	DATE OF ORIGINAL ISSUE:	2008/01/28 2008/01/31
		REVIEW/ REVISION DATE:	2009/02/23
MEDICAL DEPARTMENT/DIVISION:	NEPHROLOGY/RENAL TRANSPLANT PROGRAM AMCARE CLINIC		

DIVISION HEAD: NEPHROLOGY — DR. PETER MAGNER — DATE: YYYY/MM/DD

CATEGORY:	☒ PRESCRIPTION ☐ PROCEDURE ☒CONSULTS ☒ DIAGNOSTIC TEST ☒COMMUNICATING DIAGNOSIS
DESCRIPTION OF TREATMENT, INTERVENTION OR PROCEDURE:	Prescribing Medications. Ordering Laboratory and Diagnostic Tests. Communicating a diagnosis.
REGULATED HEALTH PROFESSIONAL(S) AUTHORIZED TO IMPLEMENT DIRECTIVE:	Janice Bissonnette RN, MScN, APN, CNCC(C)
INCLUSION CRITERIA (SPECIFIC CONDITIONS/ CIRCUMSTANCES THAT MUST EXIST):	Post Kidney transplant patients followed at the ambulatory care clinic Renal Transplant Program.
EXCLUSION CRITERIA (CONTRAINDICATIONS FOR IMPLEMENTING MEDICAL DIRECTIVE):	Consent for administration of medication, for laboratory or diagnostic test denied by patient.
DOCUMENTING THE ORDER:	The APN places a check mark (√) in the appropriate box corresponding with the diagnostic test on the transplant clinics order sheet. The APN initials the test ordered, dates and signs with full signature and designation on the order sheet, including the Medical Directive number.
MANAGEMENT OF UNTOWARD OUTCOMES:	The APN reports any untoward events related to the initiation or implementation of this medical directive to the attending Transplant Nephrologist and Dr. G. Knoll. The APN documents the event in the patient's chart. **At any time, the APN-RN does not feel comfortable carrying out the medical directive or feels the patient is unstable; he/she will consult the Physician before carrying out the Medical Directive.**
EDUCATION PROCESS: (Resources available to ensure appropriate education, as well as annual review, including evaluation).	The APN has additional training as an Acute Care Nurse Practitioner and prepared at the Master's and Post Masters level in advanced health assessment, clinical reasoning, pathophysiology and therapeutics. The APN has the knowledge, skill and judgment required to prescribe and monitor the effects of specific medications related to the management of kidney transplant patients.
COMMUNICATION PATH (A COPY OF THE FULLY SIGNED MEDICAL DIRECTIVE TO BE SENT TO MEDICAL AFFAIRS AND SENIOR VP PROFESSIONAL PRACTICE):	1. The APN communicates to the patient the purpose for the prescribed medication and any side effects related to the medication. (See appendix A) The APN documents in the patients chart any adverse drug effects experienced because of the prescribed medication. 2. The APN will communicate to the patient the purpose of the prescribed laboratory or diagnostic test. The APN reviews results, discusses significant abnormal results with the attending physician, prescribes as per appendix A..

TITLE:	**Medical Directives:** The prescribing of medications, ordering of laboratory and diagnostic tests by the APN (Advanced Practice Nurse) for Renal Transplant Clinics.	NUMBER:	RTP 4.0 Med Dir 1.00
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DIVISION HEAD: NEPHROLOGY DR. PETER MAGNER DATE: YYYY/MM/DD

	3. The Director of the Nephrology program is responsible to communicate this Medical Directive to all members of the Department (physicians), who will be delegating this directive to the APN. The physicians sign the signature page authorizing the use of the directive. 4. The APN and Clinical Director of the Nephrology program are responsible to monitor the use of this Medical Directive and to review its use on an annual basis. 5. The Clinical Director of the Program communicates this medical directive to other Regulated Health Professionals affected by this medical directive.
CONSENT	Consent obtained by APN as appropriate.
NAME(S) OF ORIGINATOR(S) OF MEDICAL DIRECTIVE:	Janice Bissonnette, Dr. Greg Knoll, Dr. Jolanta Karpinski, Marie-Josée Dêschenes (Nephrology Pharmacist)

REFERENCES:

1. ADM II-200 Medical Directives Policy the Ottawa Hospital.
2. RTP – SOP B1.100 Clinical Guidelines for Renal Transplantation at The Ottawa Hospital, rev 05-2007.
3. CPS The Canadian Drug Reference for Health Professionals, 2007.
4. College of Nurses (2007). Amended RN (EC) Drug, Laboratory and Diagnostic Test Lists. http://www.cno.org/docs/prac/062007_Rneclablist.html.
5. Danovitch, GM. Handbook of Kidney Transplantation, 4th Ed. Immunosuppressive Medications and Protocols for Kidney Transplantation, pp 72-134, 2005.
6. National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification and Stratification. American Journal of Kidney Disease, 39 :(S1), 2002.
7. National Kidney Foundation. (2004). K/DOQI Clinical Practice Guidelines for on hypertension and antihypertensive agents in chronic kidney disease. *American Journal of Kidney Disease, 43* (Suppl. 1), S1-S290.
8. National Kidney Foundation. (2004a). Clinical practice guidelines for managing dyslipidemias in kidney transplant patients: a report from the Managing Dyslipidemias in Chronic Kidney Disease Work Group of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative *American Journal of Kidney Disease, 4* (Suppl. 7), 13-53.
9. National Kidney Foundation. (2006). K/DOQI Clinical Practice Recommendations for Anemia in Chronic Kidney Disease in Renal Transplant Recipients. *American Journal of Kidney Diseases, 47* (5), S110-S116.
10. Clinical Practice Guidelines and Clinical Practice Recommendations for Diabetes and Chronic Kidney Disease American Journal of Kidney Diseases, S1-179. February 2007.
11. Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease American Journal of Kidney Diseases, (S1) May 2006.
12. Laboratory Manual: Department of Pathology and Laboratory Medicine, the Ottawa Hospital, rev. 2006.
13. Laboratory Information Handbook: Department of Pathology and Laboratory Medicine, the Ottawa Hospital, 2004.

TITLE:	**Medical Directives:** The prescribing of medications, ordering of laboratory and diagnostic tests by the APN (Advanced Practice Nurse) for Renal Transplant Clinics.	NUMBER:	RTP 4.0 Med Dir 1.00
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DIVISION HEAD: NEPHROLOGY DR. PETER MAGNER DATE: YYYY/MM/DD

Appendix A

Drug Class (Clinical System)	Indications	Contraindications /Cautions	Ordering Parameters Dose Range
Immuno-suppressant agents			
Prednisone	Reduce inflammation and suppress immune response	Easy bruising, thin skin, slow wound healing, osteoporosis, increased risk of infection, weight gain, hyperglycemia	Slow tapering Dosage 20 to 5 mg po OD
Tacrolimus	Calcineurin inhibitor	Nephrotoxicity, alopecia, HTN, PTDM	Dosage range to maintain therapeutic levels as per renal transplant clinical guidelines (2). 0.5 to 10 mg po bid
Sirolimus	TOR Inhibitor	Anemia, leukopenia, decreased wound healing 5 days to establish trough level increased lipids	Dosage range to maintain therapeutic levels as per Renal transplant clinical guidelines (2). 1mg to 10 mg po OD
Cyclosporine	Calcineurin inhibitor	grapefruit may increase cyclosporine levels -Nephrotoxicity, increased cholesterol/triglycerides, HTN, PTDM	Dosage range to maintain therapeutic levels as per Renal Transplant clinical guidelines (2). 25 to 500 mg po BID
Mycophenolate Mofetil	Selective anti-metabolite, IMPDH inhibitor	Leucopenia, anemia, thrombocytopenia	250 to 1000 mg po BID
Azathioprine	Anti-metabolite	Anemia, leukopenia, thrombocytopenia	50 to 100mg po OD
Anti-Infectives			
Antibiotics/Antimicrobials • TMP-SMX • Cephalosporin's • Macrolides • Penicillin's with Beta-Lactamase Inhibitor • Quinolones • Sulfonamides • Clindamycin	- bacterial infection - Pneumonia - Exacerbation of COPD - Urinary Tract infection - cellulitis	-calculate creatinine clearance in patients with renal dysfunction reduce dosage accordingly - Hypersensitivity/allergy to agent - Quinolones drug interaction with cyclosporine	Dosage ranges based on creatinine clearance. Antibiotic based on sensitivity to bacterial agent. Oral route.

TITLE:	**Medical Directives:** The prescribing of medications, ordering of laboratory and diagnostic tests by the APN (Advanced Practice Nurse) for Renal Transplant Clinics.	NUMBER:	RTP 4.0 Med Dir 1.00
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DIVISION HEAD: NEPHROLOGY DR. PETER MAGNER DATE: YYYY/MM/DD

Drug Class (Clinical System)	Indications	Contraindications /Cautions	Ordering Parameters Dose Range
CVS			
ACE Inhibitors	-post MI with LVEF <40% -CHF -HTN	-symptomatic hypotension if SBP<90 -Renal artery stenosis -Angioedema due to ACE or ARB use	- monitor electrolytes and renal function **Dosage based on choice of agent and adjusted to response.** **Target BP 130/80**
Angiotension II Receptor Blockers (ARBs)	-HTN -Mild-moderate CHF for patients intolerant of ACE-I & NTG/hydralazine combination or in whom beta-blockers & diuretics are contraindicated or ineffective	symptomatic hypotension if SBP<90 -Renal artery stenosis -Angioedema due to ACE or ARB use	-monitor electrolytes and renal function **Dosage based on choice of agent and adjusted to response.** **Target BP 130/80**
Beta Blockers	-Acute Coronary Syndromes -HTN -CHF -Atrial Fibrillation	-2nd or 3rd degree Heart Block -Symptomatic Bradycardia -Symptomatic Hypotension - Beta-Blockers may not be initiated in any patients with acute heart failure symptoms. -Use with caution in patients with Asthma or COPD, if a wheeze or bronchospasm develops, medication may be discontinued.	-monitor blood sugars in diabetic patients due to blunting of hypoglycemia symptoms. **Dosage based on choice of agent and adjusted to response. Oral route.** **Target BP 130/80**
Calcium Channel Blockers -dihydropyridines (DHP) -nondihydropyridines (Non-DHP)	-HTN (DHP, Non-DHP)) -Angina (DHP, Non-DHP)) -Atrial Fibrillation (Non-DHP) -SVT (Non-DHP)	-caution in CHF (DHP) -caution in diabetes (DHP) -caution in impaired liver and renal function (DHP, non-DHP) -caution when on Beta-blockers (DHP, non-DHP) -Caution in aortic stenosis (DHP) -Hypotension SBP<90 (DHP, non-DHP) - Symptomatic Bradycardia <60 (non-DHP) -Recent MI (non-DHP) -2nd or 3rd degree Heart Block (non-DHP)	**Dosage based on choice of agent and adjusted to response. Oral route.** **Target BP 130/80**

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PROGRAM:	☐ CRITICAL CARE/EMERG MED ☐ TOHRCC ☒ MEDICINE ☐ HEART INSTITUTE ☐ PSYCHIATRY ☐ OBS/GYN ☐ REHABILITATION ☐ SURGERY	DATE OF ORIGINAL ISSUE:	2008/01/28 2008/01/31
		REVIEW/ REVISION DATE:	2009/02/23
MEDICAL DEPARTMENT/DIVISION:	NEPHROLOGY/RENAL TRANSPLANT PROGRAM AMCARE CLINIC		

DIVISION HEAD: NEPHROLOGY DR. PETER MAGNER DATE: YYYY/MM/DD

Drug Class (Clinical System)	Indications	Contraindications /Cautions	Ordering Parameters Dose Range
Nitrates	-Angina -Reduction of preload	-Caution with aortic stenosis -Cerebral hemorrhage -mitral stenosis -symptomatic hypotension -head trauma -caution in patients taking sildenafil in last 24hrs – may develop hypotension refractory to vasopressors.	Limited to oral/sl/topical agents - Ensure a 10-12 hour nitrate free period to prevent development of nitrate tolerance - the ACNP will not increase the dose if patent's SBP remains <90 mmhg or demonstrates symptomatic hypotension.
Diuretics Hydrochlorothiazides Loop Diuretics -furosemide	-Heart Failure -HTN	-Severe electrolyte depletion -Oliguria/anuria -Hypovolemia -symptomatic hypotension -severe renal failure	-monitor weights, electrolytes, BUN and Creatinine. Dosage based on choice of agent and adjusted to response.
Anti-thrombotic & anti-coagulants -ECASA, ASA	-reduction of stroke, MI or vascular death	- history of recent or active GI ulcer - blood dyscrasia -suspected cerebral hemorrhage or aneurysm -hemophilia -severe liver dysfunction -uncontrolled hemorrhage -pericarditis -thrombocytopenia	ASA/ECASA 81 mg po OD
Anti-lipemic Agents - HMG-CoA reductase	-elevated lipids -secondary prevention in CVS disease -primary prevention in high risk individuals	-active liver disease -unexplained persistent elevation of serum transaminases or CPK -hypersensitivity to statins -renal insufficiency -gallbladder disease - reduce dose of statin if on CNI	**Upon initiation monitor liver enzymes prior and q 2- 4- 8 weeks.** **Target LDL $\leq$ 2.5**

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Drug Class (Clinical System)	Indications	Contraindications /Cautions	Ordering Parameters Dose Range
GI			
Histamine 2 receptor antagonists -Ranitidine Proton pump inhibitor - Omeprazole -Pantoprazole	Dyspepsia/Ulcer protective agents	-caution in impaired liver and renal function	Oral routes. Dosage based on agent chosen.
Dermatologicals			
Topical antimicrobial agents Antifungals Hydrocortisone	-Topical infection -topical fungal infection -dermatitis	Known hypersensitivity Documented bacterial infection	Topical agents only.
Metabolic/Nutrient/Fluid Replacement Agents			
Anemia Ferrous gluconate/fumerate Aranesp (Erythropoietic agent)	Iron deficiency Anemia of Chronic Disease	Known allergy/hypersensitivity Monitor Hgb q 2 week during titration, q mos when stable level achieved.	Oral route only 300 - 600 mg po qhs. Target tsat 20%, Ferritin 100ng/l s/c initiate at 40mcg q weekly, titrate to response max 100 mcg q 5 days Target Hgb 110- 120
(K <3.5) K- elixir (20 mEq/15 mL) K-Dur (20 mEq) K-Lyte (K >5.5) Sodium Polystyrene sulfonate suspension (MG < 0.7) Magnesium Rougier Magnesium Sulphate	Electrolyte imbalances Hypokalemia Hyperkalemia Hypo-magnesemia	Caution in renal insufficiency	Oral routes only. Dosage based on serum electrolyte levels. Monitor electrolytes post treatment routinely and based on response.
Tums, Tums ES Calcium Carbonate	Calcium deficiency Hyper-phosphatemia	Caution in renal insufficiency. Monitor Ca/PO4 response.	1-3 tabs po tid with meals/snacks Adjust dose to maintain Ca/Po4 within target range (P04 0.78-1.53 mmol/l) (Ca 2.23-2.58 mmol/l)

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Drug Class (Clinical System)	Indications	Contraindications /Cautions	Ordering Parameters Dose Range
Sodium Bicarbonate	Bicarb replacement Chronic Kidney Disease P CO2 < 19	Caution with fluid status, increases sodium retention.	½ - 1 tsp po od – bid (baking soda) 1-4 tabs po qid prn
Intravenous solutions 0.9%	Fluid Volume deficit Symptomatic hypotension in combination with fluid volume deficit.	Caution in known CHF, Renal Insufficiency	IV therapy for rapid re-hydration. IV 500ml bolus x 1 for noted indications.
Vitamin Folic acid Multivitamins Thiamine Replavite	Prevention & treatment of nutritional deficiencies, especially if alcohol use/abuse	Known allergy/hypersensitivity	Oral routes only.
Calcitriol	Vitamin D analog Hyperparathyroid PTH inhibition	Monitor Ca/Po4 levels, PTH levels	0.25 mcg – 1 mg po OD Adjust dosage to maintain calcium/PTH/PO4 levels within target range.
Miscellaneous			
Nonopioid analgesics Acetaminophen	Pain Management	Known allergy/hypersensitivity	Oral or PR routes as indicated
Antiemetics Dimenhydrinate Prochlorperizine Metoclopramide Domperidone	Nausea and Vomiting	Known allergy/hypersensitivity	Oral routes. Dosage based on agent.
Cathartics and laxative Docusate Sodium Hydroxide/Aluminum Hydroxide/Cascara Glycerine Suppository Bisacodyl Suppository Sodium Phosphates Enema Lactulose syrup	Constipation	Known allergy/hypersensitivity	Oral or pr routes as appropriate. Dosage based on agent.
Loperamide	Non-bacterial Diarrhea	Clostridium Difficile	4 mg loading dose, then 2 mg prn up to 16 mg/day
Allopurinol	Prevention of gout	Adjust dosage for renal failure. Monitor urate levels.	100 mg po OD and adjust to effect.

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Drug Class (Clinical System)	Indications	Contraindications /Cautions	Ordering Parameters Dose Range
Sedatives/anti-anxiety agents Lorazepam Oxazepam	Insomnia/anxiety	Known allergy/hypersensitivity Narrow angle glaucoma Sleep Apnea	Oral or s/l routes only. 2 mg po/sl q4h prn 15-30 mg po qhs
Antihistamine Diphenhydramine Epinephrine	Allergic Reaction or Prophylaxis	Known allergy/hypersensitivity	Oral, IV, IM, SQ routes as indicated.

Laboratory tests

Hematology	CBC, ESR, retic count, differential, INR, PTT
Blood Bank	ABO & Rh, Type and Screen
Biochemistry	Na, K, Cl, C02, creatinine, urea, glucose (random/fasting/2h PC), magnesium, calcium, phosphate, urate, albumin, Iron, TIBC, Ferritin, folate, Vitamin B 12, HbA1c, TSH, CK, bilirubin, ALP, AST, ALT, LD, total protein, Cholesterol, Triglycerides, HDL-cholesterol, LDL-cholesterol, PTH, urinalysis, urine/serum osmolality, urine creatinine/Na/K/Cl/protein/albumin, 24 hour urine for creatinine clearance and protein, stool for occult blood
Microbiology	Cultures of wound, blood, sputum, urine, stool, throat (nasopharyngeal),venous access sites
Virology	Blood, sputum, urine, skin, stool, nasopharyngeal
Therapeutic Drug Level Monitoring	Tacrolimus, Cyclosporine, Sirolimus, lithium, dilantin, valproate, carbamazepine, digoxin

Diagnostic Imaging	Consult Services
Chest X-ray – PA & LAT CT scan chest, abdomen and pelvis Abdominal series and flat plate Ultrasound- abdomen/pelvis ECG	Social Work Dietitian Vascular Access Peritoneal Catheter Access Endocrinology Renal Transplant Referral

Appendix V
Renal Transplant CKD Policy

Nephrology Program/Programme de néphrologie
Renal Transplant Program Standard Operating Procedures

Title / Titre: Renal Transplant Chronic Kidney Disease Clinic Process	NO.
Effective on : January 2006 Last revision / Dernière révision : February 2008	RTP SOP 2.11
Category / Catégorie : Clinical	Source: Renal Transplant Program

Approved by / Approuvé par
Renal Transplant Steering Committee Nephrology Steering Committee

POLICY

Interdisciplinary outpatient clinic process dedicated to the assessment, medical management, treatment and support of post renal transplant patients with chronic kidney disease/chronic allograft nephropathy.

PURPOSE

To describe and identify the patient process, including the assessment, planning and interventions associated with a Post Renal Transplant Chronic Kidney Disease (PRT-CKD) patient clinic visit.

BACKGROUND STATEMENTS

Primary goals: 1. Preservation of renal graft function.
2. Optimize clinical targets.
3. Optimize ESRD access preparation.

- Patients assessed and fully informed of all dialysis and transplant options.
- PRT-CKD clinic visits occur on a regular basis in the Nephrology Ambulatory Clinic setting, 1-2 half days per week, average six patients, with maximum two over-bookings.
- Patient's condition and clinician recommendation determines the frequency of PRT-CKD clinic visits.
- Advanced Practice Nurse-Nurse Practitioner (APN-NP) in consultation with the Transplant Nephrologist assesses the patient at each visit.
- Nephrology Dietitian and Social Worker assess the patient at each visit.
- Nephrology/Transplant Pharmacist assess patients on initial transfer into clinic and each visit as needed.
- Clinic Flow: Clinic visit 30-40 minutes. Recommended timing for each disciplines assessment is 10 minutes.
- Transplant CKD multidisciplinary team meeting to occur q 2 weeks to review patient's plan of care.

PROCEDURE

Section A – Transferring Patient to Post Renal Transplant CKD Clinic (NEP TRI)

- Transplant Nephrologist reviews patient clinical status based on criteria for post-transplant chronic kidney disease/chronic allograft nephropathy:
  - Serum creatinine $\geq$ 250 mmol/l or creatinine clearance <30ml/min for greater than 3 months
  - Biopsy or clinical determination of chronic allograft nephropathy
  - Absence of active acute rejection
  - Potential for dialysis or re-transplantation within one year
  - Transplant RN explains PRT-CKD clinic model to patient
  - Transplant Nephrologist or RN provides patient with return appointment time, **noting transfer to NEPTRI** (SMS code) on clinic appointment card.
  - Patient requested to complete next blood tests at least one hour prior to clinic appointment date.
  - Should patient require visits outside the PRT-CKD clinic time due to an acute medical issue, patient booked into regular transplant clinic for follow-up

SECTION B: Clinic Visit Process

Clerical:

- Ensure availability of all charts for clinic as needed 1-2 days pre-clinic.
- Ensure all charts are stocked and plaqued before clinic
- Ensure availability of most recent blood work and other diagnostic tests on chart.
- Prepare Transplant Work-up chart section as required when referral initiated
- Maintain data entry for transplant referrals as required

APN-NP Role:

- Review chart and all test results.
- Liaise with multidisciplinary team members to plan patient flow in clinic.
- Transcribe med list, asses if care plan needs updating
- Complete vital signs assessment including Ht., Wt.,
- Complete targeted nursing/medical history and physical
- Document findings on flow sheet and interdisciplinary progress notes
- Update medication list and document any changes on medication record in chart as well as on patients own record.
- Assess and review with patient treatment adherence and self-management strategies.
- Review and confirm plan of care, medication changes and investigational recommendations with Transplant Nephrologist as per medical directives
- Discuss with patient ESRD options and refer to Options teaching.
- Refer for PD access evaluation &/or Vascular access evaluation
- Refer for PD insertion or Fistula creation as determined
- Discuss and initiate Transplant Referral process as indicated
- Upon return to dialysis, document summary note in Nephrocare.

Renal Transplant Nephrologist:

- Review and approval of APN medical directives on an annual basis.
- Consultation with APN reviewing plan of care, medication changes and investigational recommendations.
- Prescriptions for medications not currently covered under the APN scope of practice as per medical directives.
- Assessment of patient as required based on APN assessment and scope of practice as per medical directive.

Dietitian's Role:

- Ensure 24hr urine available on transfer to clinic and q 6 months.
- Provide with updated dietary plan
- Review weight changes, Ca/PO4/K results with patient
- Explain urea kinetic results to patients (if appropriate for patients level of understanding)
- Assess parameters related to diet that aren't in the ideal range
- Council patients on appropriate changes needed
- Give positive feedback and encouragement with regard to parameters that are in the ideal range
- Provide information that will help them with their diets – availability of special products, renal frozen dinners, renal cookbooks
- Liaise with the other team members as needed during or after the clinic visit.

Social Worker's Role:

- Introduction to SW role; normalize SW visit as part of team approach
- Assessment and facilitation of resource access:
    - Living Situation, Support System, Transportation, Medication Coverage Finances, Palliation.
- Understanding of treatment options
- Discussion of POA/Advance directives
- Should visit require prolonged discussion due to social issues to book separate appointment with patient

Pharmacists Role:

- Interview with patients to clarify medication history, adherence and identification of drug-related-problems (DRPs)
- Provide updated medication list upon transfer to clinic and review with patient.
- Review medication profile with focus on optimizing drug dosage with renal function, administration timing and frequency and drug interactions where possible.
- Monitor drug therapy according to routine blood work, discuss if needed and document concerns related to patient self-adjustment or discontinuation of medications.
- Monitor and document adverse drug reactions
- Educate patients as needed
- Document interventions in progress notes

Documentation tools:

- Care Plan/Kardex
- Medication Flow Sheet – As per post-transplant follow-up clinic.
- APN Medical Directives for Initial and follow up orders
- Standard Physicians order form
- Multidisciplinary Progress Note
- Clinic Flow Sheet

Education Classes

- Patients considered potential candidates for repeat transplant participate in Companions Education Group Sessions.
- Referral initiated through completion of transplant referral form (Standard Physicians Orders NEP SPO 140 a, 140 b)

CQI and Clinical Outcome Indicators

Goal: Preservation of Renal Graft Function and Optimization of Clinical Targets

1. Blood Pressure control
2. Lipid management
3. Ca, Phosphate, Parathyroid hormone management
4. Anemia management

5. Diabetes management/control
6. CVD risk management
    - Smoking Cessation
    - Weight management
    - Lifestyle modification
7. Treatment adherence management
8. Referral for ESRD options teaching.
9. Referral for Peritoneal dialysis catheter/Fistula evaluation and insertion.
10. Referral for initiation of dialysis prior to acute start requirement.

Related Policy or Procedures:

1. RTP 2.1 SOP B1.100 Clinical Guidelines for Renal Transplantation at the Ottawa Hospital
2. RTP 2.2 SOP 3.15 Referral and Evaluation of the Potential Renal Transplant Recipient Procedure
3. RTP 2.3 SOP 5.500 Renal Transplant Recipient Work-up Procedure
4. RTP 2.4 SOP Nep 8.0.7 Entering and Updating Transplant Status in Nephrocare
5. RTP 3.3 SP0 48A New Referrals to Renal Transplant Program (Standard Physicians Orders)
6. RTP 3.4 SPO 48B Evaluation for Potential Renal Transplant Recipient (Standard Physicians Orders)
7. RTP 4.0 Med Dir 1.00 Medical Directives APN Renal Transplant Clinics.