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Improving medication safety and cardiovascular risk factor control to mitigate disparities in African-American kidney transplant recipients: Design and methods

Andrew J. Cole[a,1], Reginald W. Johnson II[a,1], Leonard E. Egede[b], Prabhakar K. Baliga[c], David J. Taber[d,e,*]

[a] College of Medicine, Medical University of South Carolina, Charleston, SC, USA
[b] Division of General Internal Medicine, Medical College of Wisconsin, Milwaukee, WI, USA
[c] Department of Surgery, College of Medicine, Medical University of South Carolina, Charleston, SC, USA
[d] Division of Transplant Surgery, College of Medicine, Medical University of South Carolina, Charleston, SC, USA
[e] Department of Pharmacy Services, Ralph H Johnson VAMC, Charleston, SC, USA

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ABSTRACT

There is a lack of data analyzing the influence of cardiovascular disease (CVD) risk factor control on graft survival disparities in African-American kidney transplant recipients. Studies in the general population indicate that CVD risk factor control is poor in African-Americans, leading to higher rates of renal failure and major acute cardiovascular events. However, with the exception of hypertension, there is no data demonstrating similar results within transplant recipients. Recent analyses conducted by our investigator group indicate that CVD risk factors, especially diabetes, are poorly controlled in African-American recipients, which likely impacts graft loss. This study protocol describes a prospective interventional clinical trial with the goal of demonstrating improved medication safety and CVD risk factor control in adult solitary kidney transplant recipients at least one-year post-transplant with a functioning graft. This is a prospective, interventional, 6-month, pharmacist-led and technology enabled study in adult kidney transplant recipients with the goal of improving CVD risk factor outcomes by improving medication safety and patient self-efficacy. This papers describes the issues related to racial disparities in transplant, the details of this intervention and how we expect this intervention to improve CVD risk factor control in kidney transplant recipients, particularly within African-Americans.

1. Background

The rates of graft loss for African-American (AA) renal transplant recipients are significantly higher than the rates of graft loss for non-AAs. Based on recent data, AA recipients have a 42% higher risk of graft loss at five years post-transplant and the average kidney transplant functions about half as long in AA patients [1]. Despite nearly 40 years of focused research endeavors into this disparity, little has changed in this racial inequality [1–3]. These disparities have primarily been attributed to immunologic risks leading to higher rejection rates [4–7], lower socioeconomic status (SES) [8,9], medication non-adherence [10,11], and comorbidities [12–14].

AA renal transplant recipients have more robust immunologic responses, placing them at higher risk for acute rejection. These include more MHC polymorphisms [15], pre-sensitization to MHC antigens [16], greater HLA mismatches [17], immune hyper-responsiveness [18], and cytokine polymorphisms [19,20]. Therefore, most of the early work trying to eliminate outcome disparities in AA patients was appropriately focused on reducing acute rejection rates through immunosuppressant pharmacotherapy [21,22]. Though the acute rejection rate has decreased, the graft loss disparity within the AA patient population remains the same [22–24]. Studies evaluating the influence of SES and medication adherence on racial disparities in kidney transplant recipients have produced conflicting results, with some studies suggesting SES and medication adherence may influence racial disparities, while other resulted in contradictory findings [25–30].

In terms of cardiovascular disease (CVD) and CVD risk factors, AA kidney transplant recipients have nearly twice the rate of diabetes

* Corresponding author. Division of Transplant, Surgery Medical University of South Carolina, 96 Jonathan Lucas Street, MSC 611, Charleston, SC 29425, USA.
E-mail addresses: coleand@musc.edu (A.J. Cole), johnsreg@musc.edu (R.W. Johnson), legede@mcw.edu (L.E. Egede), baligap@musc.edu (P.K. Baliga), taberd@musc.edu (D.J. Taber).
[1] Co-lead authors.

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Abbreviations

AA	African-American
ADA	American Diabetes Association
BP	Blood pressure
CRF	Case report form
CTCAE	Common terminology criteria for adverse events
CV	Cardiovascular
CVD	Cardiovascular disease
DSMP	Data safety monitoring plan
eGFR	Estimated glomerular filtration rate
HIPAA	Health Portability and Accountability Act
HbA_{1C}	Hemoglobin A1c
IRB	Institutional review board
LDL	Low density lipoprotein
MHC	Major histocompatibility complex
mmHg	Millimeters of mercury
NIH	National Institutes of Health
REDCap	Research Electronic Data Capture
SES	Socioeconomic status
VA	Veterans Affairs

[31–33] and four times the rate of hypertension [12,33] as compared to non-AA recipients. Data from the general population suggests that both hypertension and diabetes occur at an earlier age, are of a more aggressive phenotype and more likely to lead to end-organ damage in AA patients [34–36].

Unfortunately, there is a lack of data analyzing the influence of CVD risk factor control on graft survival disparities in AA transplant recipients. Studies in the non-transplant population indicate that CVD risk factor control is poor in AA patients, leading to higher rates of renal failure and CV events [37]. However, with the exception of hypertension [38], there is paucity in data demonstrating similar results within transplant recipients [39].

Recently, using VA data, we have also demonstrated that CVD risk factor control is lower in AA kidney transplant recipients and that it is a substantial explanatory variable for racial disparities [40]. This clinical trial study stems directly from these retrospective studies. Once completed, this trial will provide empirical evidence demonstrating the feasibility and exploring the potential effectiveness of pharmacist-led interventions to improve medication safety and CVD risk factor control within kidney recipients; while also demonstrating the potential improvements in CVD risk factor control more substantially within AA recipients.

2. Methods/Design

2.1. Study design

This is a prospective, clinical trial assessing the potential efficacy of a 6-month, pharmacist-led, technology enabled education intervention on improving medication safety and cardiovascular risk factor control in adult solitary kidney transplant recipients with a secondary aim of assessing if the impact of intervention varies by race. The primary objectives include determining if the study is feasible, as measured proportions of enrolled to approached and completed to enrolled,

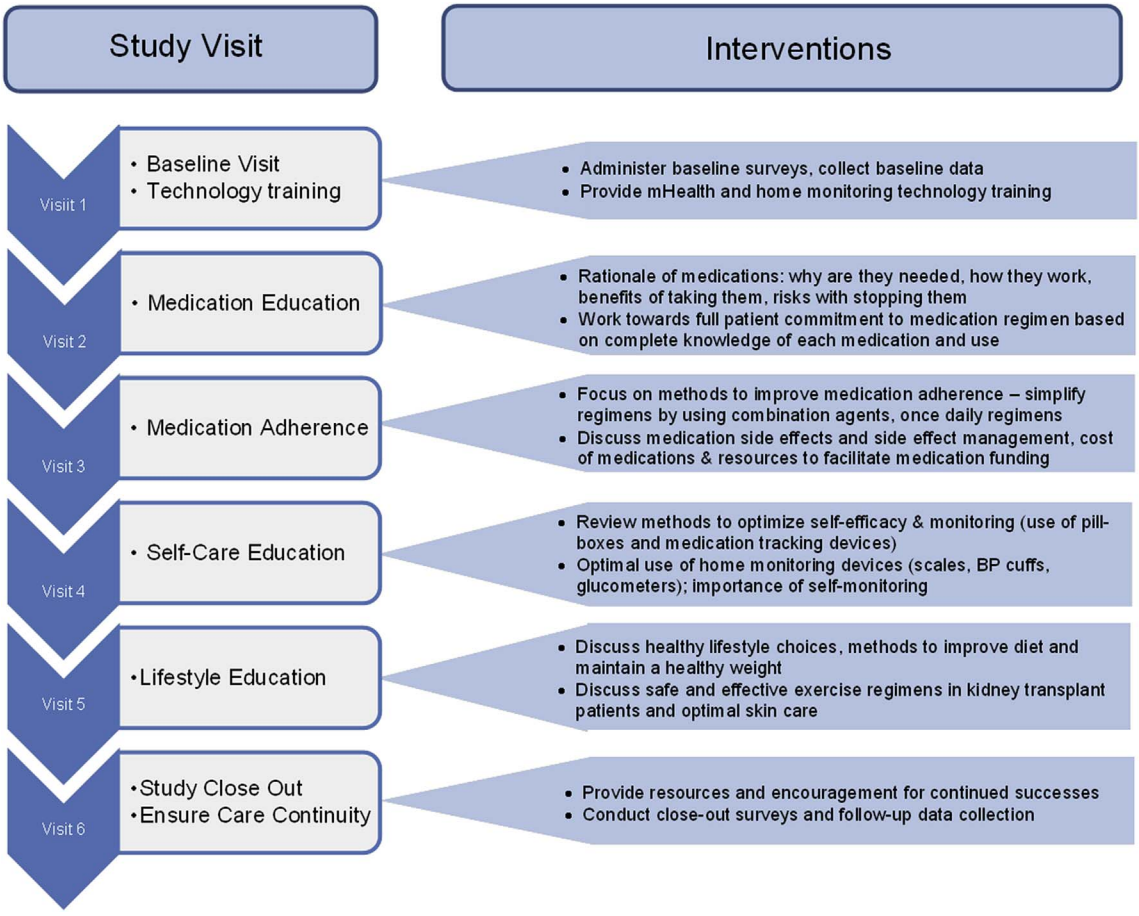

Fig. 1. Legend – Schematic of 6 monthly visits with details of the activities and interventions occurring at each visit.