The proposed application will investigate whether initiating treatment with ultra-low-dose quadruple-combination therapy (LDQT; including irbesartan 37.5 mg, amlodipine 1.25 mg, indapamide 0.625 mg, and bisoprolol 2.5 mg) will lower automated office blood pressure and 24-hour ambulatory blood pressure at 12 weeks more effectively, and with no increase in side effects, compared to initiating standard dose monotherapy (irbesartan 150 mg) in adults with raised blood pressure (SBP>130 mmHg or DBP>80 mmHg) and without cardiovascular disease. Our preliminary data from a short-term (4-week) crossover trial of 18 participants suggest that LDQT lowers office blood pressure by 22/13 mmHg on average compared with placebo with no difference in serious adverse events. Effects on 24-hour ambulatory blood pressure were similar.

We will perform this phase II, single site, randomized controlled trial in a network of federally qualified health centers in Chicago because this population bears a disproportionate burden of blood pressure related diseases, and we have previously successfully conducted clinical studies in this population. This new and simpler treatment paradigm has potential to eliminate blood pressure disparities in this population, which provides the motivation for this proposal. While we hypothesize this intervention will be easily implemented and efficacious for all patients and clinicians, we will explore variation in treatment effect by potential moderating variables, including age, sex, race/ethnicity, and health literacy level. Beyond examining efficacy, we also plan to assess feasibility of implementing this intervention in a clinical setting by simultaneously evaluating implementation outcomes of acceptability, preferences, and lessons of LDQT among patients and clinicians.

Two early stage investigators will lead the study team with relevant, complementary clinical trial experience in cardiovascular medicine and biostatistics, which provide a strong foundation for this proposal. Our team will leverage internal and external experience and resources in cardiovascular research, combination drug therapy, and implementation science to study a novel intervention in a high-burden, low-resource population from a single site through this phase II trial. We plan to pool the present trial data with that of similar trial conducted in Australia (led by one of the study team members in this proposal) to examine the robustness and generalizability of our study results.

This proposal aims to create, evaluate, and demonstrate successful implementation of an ultra-low dose quadruple combination drug therapy that is simpler, more efficacious, and safer than standard therapy for patients and their doctors. If successful, then the proposal will lay the framework for a larger multi-site phase III randomized controlled trial with goal of confirming efficacy and safety in a larger population, with the ultimate goal of a complete change the paradigm for initial blood pressure lowering therapy.