

Wills Eye Health System

Annual Progress Report: 2009 Nonformula Grant

Reporting Period

July 1, 2013 – May 31, 2014

Nonformula Grant Overview

The Wills Eye Health System received \$3,598,366 in nonformula funds for the grant award period June 1, 2010 through May 31, 2014. Accomplishments for the reporting period are described below.

Research Project: Project Title and Purpose

Confronting Unequal Eye Care in Pennsylvania - The purpose of this research project is to increase utilization of eye care for older African Americans with diabetes and to provide research training and mentoring for minority students. We are conducting a randomized, placebo-controlled clinical trial to test the efficacy of a culturally-relevant intervention, Behavioral Activation, to increase the rates of dilated fundus examinations in this population. We also developed a vision research training and mentoring program to increase minority nursing and biomedical students' vision research skills.

Duration of Project

6/1/2010 - 5/31/2014

Project Overview

The project's overarching goals are to increase older African Americans' utilization of eye care and to promote minority students' interest in pursuing research careers. Older African Americans with diabetes are more likely than older Caucasians with diabetes to develop severe vision loss from diabetic retinopathy (DR), which is a major complication of diabetes. Early detection with annual dilated fundus exams (DFEs) can prevent severe vision loss resulting from DR. However, African Americans are less likely to have DFEs than Caucasians. To reduce this health disparity, we propose the following Specific Aims:

1. To conduct a randomized, placebo-controlled clinical trial to test the efficacy of Behavior Activation (BA) to increase rates of DFEs in older African Americans with diabetes. The control treatment, Supportive Therapy (ST), is a placebo interaction to control for the interpersonal attention that subjects randomized to BA will receive. Both interventions are conducted in subjects' homes. We will enroll 206 older African Americans with diabetes who have not had a DFE in the past year and randomize 50% to each treatment group in this 6 month clinical trial. We hypothesize that 60% of subjects who receive BA compared to 35% of subjects who receive

ST, will schedule and obtain a DFE by 6 months. Secondary outcome measures include knowledge of the risk of diabetes complications, adherence to diabetes self-care recommendations, and depressive symptoms. We will also examine the long-term efficacy of BA annual DFE rates.

2. To develop a Minority Research Training and Mentoring Program at the Wills Eye Health System to increase research skills and promote interest in pursuing research careers for undergraduate and graduate minority nursing and biomedical students. To accomplish Aim 2, we will create a minority training program and summer research internship for up to four minority students per year.

Principal Investigator

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Benjamin Leiby, PhD; Kathy Ashton, PhD; Laura Pizzi, PharmD (Thomas Jefferson University)
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Expected Research Outcomes and Benefits

This research project will have both immediate and long-term outcomes. The immediate outcome is two-fold. First, we will determine the efficacy of an innovative, culturally relevant home-based intervention to increase rates of diabetic eye screening in older African Americans. We know that many patients in this population do not fully understand diabetic eye disease or how to access care to identify or prevent it. Our research will test a program to increase utilization of ophthalmic care, thereby reducing African Americans' risk for vision loss and blindness which is a pervasive health disparity. The research project's second immediate impact is that we will increase the research skills of a cadre of undergraduate and graduate minority nursing and biomedical students through direct participation in our research projects and research training programs. We will accomplish this via a research training program that consists of a summer research internship with didactic and hands-on training as well as individual student mentoring. The ultimate goal is to promote minority nursing and biomedical students' interest in pursuing research careers as another step towards reducing health disparities.

The long-term impact of our work will be to prevent unnecessary suffering and disability in an underserved population at high risk for vision loss. If our efforts are successful, they will reduce

costs associated with vision loss and its complications (e.g. depression, falls and fall-related injuries, and nursing home placements). Ultimately, the intervention that we are testing can serve as a broad-based, community health model for other medical conditions that disproportionately affect African-Americans such as asthma, hypertension, and prostate cancer, where treatment adherence is low. In this way, our translational research project's impact may extend well beyond the treatment of disorders of the eye. Our results have the potential to provide important new information to patients, clinicians, and policy makers about interventions that have the potential to save money using low cost, culturally relevant, community-based interventions.

Summary of Research Completed

This annual report covers project activities undertaken from July 1, 2013 – May 30, 2014. Our activities for Aim 1 have focused on implementing the research protocol at Wills Eye Health System, Thomas Jefferson University (TJU), and Temple University (TU). These activities include administering study treatments to enrolled subjects, performing follow-up assessments, and developing presentations and publications of available results. For Aim 2, we implemented the Clinical Vision Research Training and Mentoring Program for Minority Students in the summer of 2013. We have also created the Wills Vision Research Training and Mentoring Program for the summer of 2014.

Specific Aim 1:

Protocol Re-approval Specific Aim 1: To test the comparative effectiveness of two different, culturally relevant interventions (in-home behavior activation vs. telephone problem-solving) to increase rates of dilated fundus examinations (DFE) in older African Americans (AAs) with diabetes in a randomized clinical trial (RCT).

The Wills Eye Hospital IRB approved the continuation of Aim 1 on March 19, 2014, and TU IRB re-approved the study for an additional year on April 11, 2014. We requested approval because we continue to make follow-up telephone calls to patients, review and analyze data for primary, secondary and exploratory aims, and prepare manuscripts.

Recruitment and Retention: As of May 30, 2014, 179 subjects have completed all 4 of either Behavior Activation (BA) or Supportive Therapy (ST) sessions in addition to a 6-month follow-up assessment. Our target number, accounting for a 20% attrition rate, was 164 subjects. One hundred and thirty one (131) subjects have completed 1-year follow-up assessments and 97 subjects have completed 18-month follow-up assessments.

Study Outcomes: Our primary hypothesis for Aim 1 is that a greater proportion of subjects who receive BA will have a dilated eye examination by 6 months compared to subjects who receive ST. The primary outcome measure is medical documentation of a dilated fundus examination (DFE). During the 6-month follow-up assessment, all subjects were asked if they obtained a DFE and verification is obtained by reviewing medical records. Subjects who dropped from the study and are missing follow-up data at 6 months will be excluded from analysis. Primary outcome results are shown in Table 1. Of the 91 BA subjects who completed a 6-month follow-up, 88% (80 subjects) have medical documentation of a DFE. In the ST group, 30 out of 88

subjects (34%) had documentation of a DFE. Ophthalmology characteristics of participants who obtained a DFE can be found in Table 2.

Secondary hypotheses for Specific Aim 1 include:

- a) subjects who receive BA will increase their risk perception and risk knowledge of diabetes and its complications to a greater extent compared to subjects who receive ST at 6 months;
- b) subjects who receive BA will increase their adherence to diabetes self-care recommendations to a greater extent compared to subjects who receive ST at 6 months;
- c) subjects who receive BA will have lower levels of depressive symptoms compared to subjects who receive ST at 6 months.

Secondary outcomes are measured by the Risk Perception Survey for Diabetes Mellitus (RPS-DM), the Diabetes Self Care Inventory – Revised (SCI-R), and the Patient Health Questionnaire (PHQ-9). The means for these secondary outcomes at baseline by treatment group can be found in Table 3 and Table 4. Mixed effects linear regression was used to analyze these secondary hypotheses. Fixed effects included treatment group assignment, time (0 and 6 months) and group by time interaction. A random intercept term was included to account for within-subject correlation. Within the mixed effects model we estimated the change in these outcomes from 0 to 6 months for each treatment arm and compared BA to ST with respect to this change. There were no significant results between the two groups in respect to the secondary hypotheses.

One exploratory hypothesis for Aim 1 is that subjects who receive BA will have a larger reduction in A1C levels from baseline to 6 months compared to subjects who receive ST. Using the statistical analysis described previously, there was no difference between the two groups in regards to A1C from baseline to 6 months. Additionally, we have added a cost analysis of the intervention as part of our exploratory aims in response to the Interim Performance Review.

Exploratory Aims for Specific Aim 1:

Exploratory Aim 1: To examine the long-term efficacy of BA to increase rates of annual DFEs one year after the treatment intervention. This analysis has not yet been conducted.

Exploratory Aim 2: To examine whether changes in knowledge of the risk of diabetes complications, adherence to diabetes self-care recommendations, and/or depression mediate the relationship between treatment assignment and obtaining a DFE. This analysis has not yet been conducted.

Exploratory Aim 3: To examine whether differences in cultural characteristics at baseline moderate the relationship between treatment assignment and obtaining a DFE. This analysis has not yet been conducted.

Exploratory Aim 4: To examine whether a higher proportion of subjects who receive the in-home intervention will have a 1% reduction in hemoglobin A1c levels from baseline to 6 months than subjects who receive the telephone intervention. Forty-four of the 82 BA participants who allowed their A1Cs to be performed at six-months had a result below 7% compared to 31 out of the 85 ST participants (53.7% vs. 36.5%, X^2 , $p=0.026$). BA subjects had slightly lower A1Cs at

baseline, and after adjustment for baseline A1C, the difference in the proportion of participants with A1C below 7% was not statistically significant (RR=1.25; 95% CI: (0.94, 1.65); p=0.12).

Exploratory Aim 5: Conduct a cost effectiveness analysis of behavior activation versus supportive therapy in older African Americans with diabetes to increase rate of annual eye exams. This aim has been completed and the research project report is presented below.

Research Progress Exploratory Aim 5: Cost Effectiveness Analysis of Behavior Activation Versus Supportive Therapy in Older African Americans With Diabetes to Increase Rate of Annual Eye Exams.

Objective: A cost-effectiveness analysis was performed alongside a randomized clinical trial comparing Behavior Activation (BA) to Supportive Therapy (ST) (placebo condition) in promoting healthy management of diabetes and encouraging patients to schedule and receive a dilated fundus exam (DFE).

Methods: 103 subjects were enrolled in each of two groups receiving either BA or ST between 2009 and 2013. BA, the active intervention, focused on encouraging subjects to schedule a DFE using a behavioral intervention. ST, a control condition, was used to control for the individualized attention that subjects randomized to active treatment received. The interventions took place over 6 months. The primary measure for the cost analysis was incremental cost effectiveness ratio (ICER) of BA vs. ST at 0-6 months. Costs consisted of total intervention costs for each group: 1) human time costs for screening, intervention, travel, supervision, training, and alerts; 2) materials; and 3) mileage. Effectiveness measures tested in the ICER were 1) incremental cost/% of subjects receiving a DFE, incremental cost/HbA1c improvement, and incremental cost/NEI VFQ-derived quality-adjusted life years (QALY). Sensitivity analyses were performed by inputting costs and effectiveness parameters into TreeAge Pro decision analytic software.

Results: 80 of 91 subjects enrolled in BA received DFEs, compared with only 30 of 87 in ST. Data analysis performed during the reporting year showed there was no significant difference between groups in either change in HbA1c or QALY. Total costs for BA and ST per participant were \$259.02 and \$216.12 respectively. The ICERs for BA vs. ST were as follows: \$89.23/% of subjects with DFE and \$476.67/point HbA1c decrease. In terms of improving DFE rates, BA is more cost-effective than ST.

Specific Aim 2: The Minority Vision Research Training and Mentoring Program was completed in 2013 and is not included in this annual report. The full report of this program is described in the Final Progress Report.

Research Progress for Pilot Study #1: Preventing Progression of DR in Older African Americans with Diabetes (added to project July, 2012)

Specific Aims: The purpose of this pilot study was to test the feasibility of administering an in-home behavioral intervention to older African Americans who have diabetes.

Data analysis was performed during the reporting year for pilot study data. All participants were African American. The mean age was 73.7 years (SD 5.8); 92% were women. All but one participant received all 6 BA treatment sessions. Participants' mean rating of satisfaction with BA was 9.4 (SD .80) on a scale of 1 to 10 (10 = "very satisfied"). At baseline and follow-up at 8 weeks, participants rated the frequency of their adherence to DSM behaviors (1 "never" to 5 "always") on the Diabetes Self-Care Inventory-Revised (DSCI-R). Mean DSCI-R scores improved from 38.9 (9.7) to 44.9 (5.4); $t = -4.5$; $p \leq .001$. **Figure 1** depicts increases in mean scores of 5 representative DSM behaviors and the percent of participants who increased adherence by at least one level of frequency (e.g., "sometimes" to "regularly").

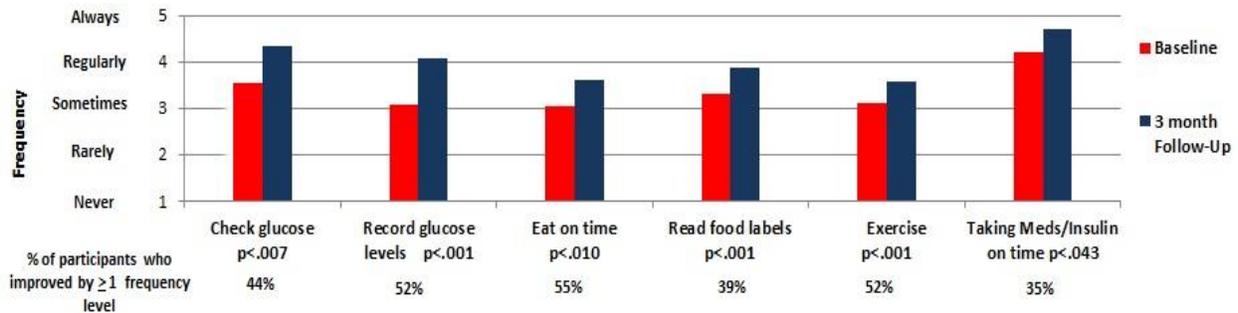


Figure 1: Change in 5 Representative DSCI-R DSM Behaviors (N = 23)

Research Progress Report for Pilot Study #2: Improving Access to Eye Care in Patients with Glaucoma (added to project May, 2013)

Following approval from the PA Department of Health, our research team developed a prospective, randomized pilot study utilizing information from electronic medical records to address follow-up adherence and reduce the gap between recommended and actual follow-up adherence in patients with glaucoma. Specifically, we evaluated the impact of a telephone-based, educational intervention on follow-up adherence in patients with glaucoma using usual care as a control.

Two-hundred and fifty-six (256) patients who were scheduled to return for follow-up eye care between September 1, 2013 to November 30, 2013 were assigned to the usual care group (126) or the telephone intervention group (130). Adherence to timely follow-up care in the usual care group was 69% compared to 82% in the intervention group. The relative risk of timely adherence in the intervention group was 1.23 (95% CI [1.08, 1.41]; $p=0.002$), indicating a 23% increase in adherence to follow-up care compared to the usual care group. The full report of this study is described in the Final Progress Report.

Disseminating Results

Based on our preliminary results, we have submitted 3 posters for presentation at national conferences and are developing 8 manuscripts for peer review submission. "Feasibility and acceptability of supportive therapy as an attention control condition for randomized controlled trials of behavioral interventions" has been written and prepared for submission to *Behavior Modification*. The primary outcome paper entitled "Behavior activation improves rates of

dilated fundus examinations in older African Americans with diabetes” has been written and prepared for submission to *Ophthalmology*. An article on recruitment titled “Recruitment strategies for older African Americans with diabetes: Opt-in versus opt-out” has been submitted to *SAGE Open*. A paper detailing the cost of the intervention has been initiated. Additional manuscripts are also being developed on the Effectiveness of Behavioral Activation; Improving Access to Eye Care in Patients with Glaucoma; and The Vision Research Training and Mentoring Program Outcomes.

The following is a list of accepted presentations in 2013:

Weiss DM, Hark LA, Leiby B, Murchison AP, Haller JA. Impact of diabetes on vision-related quality of life: Findings from a clinical trial of African-Americans. Poster presentation on November 5, 2013 at the 2013 American Public Health Association Annual Meeting, Boston, MA.

The following is a list of accepted presentations in 2014:

Leiby BE, Weiss DM, Murchison AP, Casten RJ, Hark LA, Haller JA. Ocular disease incidence and factors that influence DFE adherence in African Americans with diabetes. Poster presentation on May 7, 2014 at the 2014 Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting, Orlando, FL.

Tran J, Waisbourd M, Weiss DM, Murchison AP, Katz LJ, Spaeth GL, Haller JA, Hark LA. The effectiveness of a tailored intervention to increase follow-up adherence in patients with glaucoma. Poster presentation on May 8, 2014 at the 2014 Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting, Orlando, FL.

Table 1: Primary Outcome by Treatment Group

	BA Participants (n=91)	ST Participants (n=88)	P-value
	%	%	
Self-Reported DFE	78 (85.7)	45 (51.1)	≤ 0.001
Medical Documentation (Verified)	80 (87.9)	30 (34.1)	≤ 0.001

DFE=dilated fundus examination; BA=behavioral activation; ST=supportive therapy

Table 2: Ophthalmology Characteristics of Subjects who had a DFE by 6 Months by Treatment Group

	TOTAL (n=110)		BA (n=80)		ST (n=30)	
	N	%	n	%	n	%
History of Cataract Surgery	17	16.5	13	16.3	4	13.3
Diagnosis of DR	15	14.6	15	18.8	3	10.0
Diabetic Retinopathy (DR) Stage (Right Eye)						
Mild non-proliferative DR	14	12.7	12	15.0	2	6.7
Moderate non-proliferative DR	1	2.0	1	1.2	0	0
Severe non-proliferative DR	0	0.0	0	0	0	0
Proliferative DR	2	1.8	1	1.2	1	3.3
Diabetic Retinopathy (DR) Stage (Left Eye)						
Mild non-proliferative DR	14	14.3	12	15.0	2	6.7
Moderate non-proliferative DR	1	1.0	1	1.2	0	0
Severe non-proliferative DR	0	0	0	0	0	0.0
Proliferative DR	2	1.8	1	1.2	1	3.3
Cataracts (Right Eye)						
Grade 1	19	17.2 13	16.3	6	20.0	
Grade 2	32	29.1	25	31.3	7	23.3
Grade 3	10	9.1	8	10.0	2	6.7
Grade 4	2	1.8	2	2.4	0	0.0
Cataracts (Left Eye)						
Grade 1	22	20.0	15	18.8	7	23.3
Grade 2	35	31.2	28	35.0	7	23.3
Grade 3	8	7.3	7	8.8	1	3.8
Grade 4	4	3.6	2	2.4	2	6.7
Other Diagnoses (Right Eye)						
Hypertensive Retinopathy	10	9.1	8	10.0	2	6.7
Posterior Vitreous Detachment	11	10.0	7	8.8	4	13.3
Drusen	7	6.7	6	7.5	1	3.8
Macular Edema	1	0.9	1	1.2	0	0.0
Other Diagnoses (Left Eye)						
Hypertensive Retinopathy	9	8.2	7	8.8	2	6.7
Posterior Vitreous Detachment	11	10.0	6	7.5	5	16.7
Drusen	7	6.7	6	7.5	1	3.3
Macular Edema	2	1.8	2	2.4	0	0.0

DR=diabetic retinopathy; DFE=dilated fundus examination; BA=behavioral activation; ST=supportive therapy

Tables 3 and 4: Secondary Outcomes: BA vs. ST Subjects: 6-Month Follow-up

Behavioral Activation (n=91)								
	Missing	Mean	SD	Min	Max	25%	50%	75%
Risk Perception Scale for Diabetes Mellitus (RPS-DM)								
Risk Knowledge ¹	3	3.56	1.48	0.00	5.00	3.00	4.00	5.00
Perceived Personal Control ²	2	3.12	0.52	1.75	4.00	2.75	3.00	3.50
Worry ³	1	2.99	0.75	1.00	4.00	2.50	3.00	3.50
Optimistic Bias ⁴	4	2.25	0.85	1.00	4.00	1.50	2.50	3.00
Personal Disease Risk ⁵	2	2.66	0.78	1.11	4.22	2.06	2.78	3.22
Environmental Risk ⁶	2	2.41	0.76	1.00	4.00	1.78	2.44	2.89
Composite Score	6	2.70	0.40	1.59	3.48	2.45	2.75	2.98
Diabetes Self-Care Inventory – Total Score⁷	1	60.64	13.74	23.00	90.75	51.50	62.50	70.50
PHQ – Symptom Score⁸	2	5.29	4.97	0.00	21.00	1.00	3.00	9.00
A1c Result	9	7.05	1.33	4.10	12.00	6.10	6.80	7.53

Supportive Therapy (n=85)								
	Missing	Mean	SD	Min	Max	25%	50%	75%
Risk Perception Scale for Diabetes Mellitus (RPS-DM)								
Risk Knowledge ¹	2	3.73	1.31	0.00	5.00	3.00	4.00	5.00
Perceived Personal Control ²	2	3.13	0.58	1.00	4.00	2.75	3.25	3.50
Worry ³	0	2.87	0.70	1.00	4.00	2.50	3.00	3.50
Optimistic Bias ⁴	2	2.22	0.71	1.00	4.00	2.00	2.00	3.00
Personal Disease Risk ⁵	1	2.81	0.81	1.43	4.44	2.11	2.78	3.42
Environmental Risk ⁶	1	2.50	0.70	1.11	4.00	2.00	2.39	3.00
Composite Score	5	2.70	0.38	1.55	3.58	2.40	2.70	2.96
Diabetes Self-Care Inventory – Total Score⁷	1	59.16	15.05	27.50	93.75	50.00	60.50	68.75
PHQ – Symptom Score⁸	0	5.76	4.81	0.00	19.00	2.50	4.00	7.50
A1c Result	3	7.67	1.73	5.10	13.00	6.48	7.40	8.43

¹ Scores range from 0 to 5 with higher scores indicating greater knowledge of diabetes complications.

² Scores range from 1 to 4 with higher scores indicating more perceived control and less perceived risk over diabetes complications.

³ Scores range from 1 to 4 with higher scores indicating more worry.

⁴ Scores range from 1 to 4 with higher scores indicating more optimistic bias; lower scores indicating greater realism/pessimism.

⁵ Scores range from 1 to 5 with higher scores indicating greater perceived personal disease risk.

⁶ Scores range from 1 to 4 with higher scores indicating greater perceived environmental risk.

⁷ Scores range from 0 to 100 with higher scores indicating greater adherence to self-care recommendations.

⁸ Possible scores range from 0 to 27, with higher scores indicating worse depressive symptoms.

DM=diabetes mellitus; BA=behavioral activation; ST=supportive therapy; PHQ=patient health questionnaire