




## Program ACTIVE II: A Comparative Effectiveness Trial to Treat Major Depression in T2DM





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  - Ziyi Yang, M.S. – No COI/Financial Relationship to disclose
  - Yegan Pillay, Ph.D. – No COI/Financial Relationship to disclose
  - Karen Fitzpatrick, M.D. – No COI/Financial Relationship to disclose
  - Kieren Mather, M.D. – Consultant – Merck; Funding – NIH, Novo Nordisk (IIS); Study materials – Novo Nordisk, Sanofi, Abbott, Merck
  - Jay H. Shubrook, D.O. – Consultant, Eli Lilly, NovoNordisk, Intarcia
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## Depression in Diabetes: Prevalence

- ▶ Depression is 2 times more likely in people with diabetes than the general population (Anderson, et al., *Psychosomatic Med.*, 2001)
- ▶ 1 in 4 people with diabetes will have depression in their lifetime (Anderson, et al., *Psychosomatic Med.*, 2001; Neftci et al., 2012)
  - Depressive symptoms: 21%-27%
  - Depressive disorders: 11%-15%
- ▶ Women with diabetes have 60% increased risk of depression (Anderson et al, *Psychosom Med.*, 2001)
- ▶ Comparable rates of depression across ethnic groups with diabetes (de Groot, et al., *Diabetes Care*, 2007)



## Impact of Depression and Diabetes

- ▶ Worsened glycemic control (Lustman, et al., *Diabetes Care*, 2000)
- ▶ Greater severity of diabetes complications (de Groot, et al., *Psychosomatic Medicine*, 2001)
- ▶ Decreased adherence to diabetes treatment regimens and increased medical COSTS (Egede, et al., *Diabetes Care*, 2002; Ciechanowski, et al., *Arch Intern Med*, 2000)
- ▶ Increased functional disability (Egede, *Gen Hosp Psychiatry*, 2007)
- ▶ Increased rates of premature all-cause mortality (Katon, et al., *JGIM*, 2008; Zhang, *Am J Epidemiology*, 2005)



## Effective Treatments for Depression: Cognitive Behavioral Therapy

- Cognitive Behavioral Therapy (Lustman, et al., *Arch Intern Med*, 1998)
  - Randomized controlled trial (N=50): CBT vs. Diabetes Education for type 2 adults
  - 85% remission rate at end of intervention in the CBT arm
  - 70% remission rate at 6-month follow-up
  - 0.7% decrease in HbA1c at 6 month follow-up
- TEAM Care Studies (Katon, et al., *NEJM* 2012; Johnson et al., *Diab. Care*, 2014)
  - Primary care-based problem-solving therapy
  - Improvements in depression outcomes; mixed findings in terms of A1c outcomes

## Exercise as a Treatment for Diabetes and Depression

- ▶ Exercise has been demonstrated to be effective in treating depression among non-diabetes patients (Boule, 2000; Blumenthal, et al., *NEJM*, 1999; Babyak, *J. Psychosomatic Res*, 2000; Krogh et al., *J. Clin. Psychiatry*, 2009)
- ▶ VA Walking Study (Piette, et al., *Medical Care*, 2011)
  - 291 Veterans with elevated depressive symptoms randomized to telephone-based counseling and walking vs. usual care (UC)
  - Improvements in depression (58% treatment group vs. 39% UC)
  - No change in A1c







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Vital Exercise

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### Study Aims



1. To assess the comparative effectiveness of cognitive behavioral therapy and exercise individually and in combination compared to usual care (UC) on depression diagnosis from baseline to post-intervention.
2. To assess the comparative effectiveness of the treatment arms on glycemic control (A1c) outcomes from baseline to post-intervention.

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### Methodology and Design



- 2X2 factorial repeated measures design:
  - Cognitive behavioral therapy (yes/no) X Community-based exercise (yes/no)
- 4 Assessment Time Points:
  - **Baseline**
  - **Post-Intervention (POST)**
  - 6-Month Follow-Up
  - 12-Month Follow-Up
- ▶ Three Intervention Sites:
  - Indiana University (Indianapolis)
  - Ohio University (southeastern Ohio/western West Virginia)
  - West Virginia University (North-central West Virginia)

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### Interventions




Randomization to 4 Study Arms (N=140):

- Usual Care (N=36)
- Cognitive Behavioral Therapy (CBT; N=36)
  - 10 individual sessions with a licensed community therapist
- Exercise (N=34)
  - 12 weeks community-based exercise + 6 classes led by personal trainers
- CBT + Exercise (N=34; 12 weeks concurrent interventions)

- All participants were offered a nutrition education program: *Dining with Diabetes*

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### Eligibility Criteria



- Inclusion criteria:
  - Age 21 or older
  - Diagnosis of type 2 diabetes (duration  $\geq$  1 year)
  - Ambulatory; medically appropriate for mild to moderate physical activity
  - Current Major Depressive Disorder (primary psychiatric diagnosis)
- Exclusion criteria:
  - History of diabetic ketoacidosis
  - Continuous insulin therapy since T2DM diagnosis
  - Stage 2 hypertension as defined by JNC VII

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### Exclusion Criteria



- Recent cardiac events (e.g., unstable angina, diagnosed angina, PTCA, any cardiac intervention for CAD or tachyarrhythmias in the past 12 months)
- Laser surgery for proliferative retinopathy in the past 6 months
- History of stroke, lower limb amputation, sensory peripheral neuropathy, aortic stenosis or other severe valvular heart disease, atrial fibrillation, severe COPD (e.g., basal oxygen), class III or IV heart failure or medical instability. No lifetime history: psychotic disorders, suicide attempt, bipolar disorder
- No current psychotherapy treatment for depression
- If prescribed antidepressant medications, no change in medication or dosage within the previous 6 weeks

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### Results: Baseline Demographics

Outcome	EXERCISE				P Value
	CBT (N=36)	CBT+EXERCISE (N=34)	EXERCISE (N=34)	USUAL CARE (N=36)	
Age in years, Mean (SD)	57.9 (10.9)	57.1 (10.7)	54.6 (10.7)	54.2 (10.4)	0.367
Female	26 (72.2)	28 (82.4)	26 (76.5)	27 (75.0)	0.788
White	27 (79.4)	25 (78.1)	25 (75.8)	22 (62.9)	0.376
Marital Status					0.935
Now Married	19 (52.8)	14 (41.2)	20 (58.8)	20 (55.6)	
Never Married	5 (13.9)	7 (20.6)	4 (11.8)	5 (13.9)	
Divorced	8 (22.2)	9 (26.5)	5 (14.7)	7 (19.4)	
Separated/Widowed	4 (11.1)	4 (11.8)	5 (14.7)	4 (11.1)	
Education					0.066
<High School	13 (36.1)	7 (20.6)	5 (14.7)	3 (8.3)	
Trade School/Part College	8 (22.2)	14 (41.2)	15 (44.1)	13 (36.1)	
4 Year College or higher	15 (41.7)	13 (38.2)	14 (41.2)	20 (55.6)	
Income					0.823
< \$20,000	7 (20.6)	8 (25.0)	9 (27.3)	9 (26.5)	
\$21,000 - \$40,000	14 (41.2)	13 (40.6)	10 (30.3)	9 (26.5)	
\$41,000 - \$60,000	6 (17.7)	4 (12.5)	8 (24.2)	5 (14.7)	
> \$61,000	7 (20.6)	7 (21.9)	6 (18.2)	11 (32.4)	
Health Insurance (Yes)	30 (88.2)	29 (90.6)	30 (90.9)	29 (82.9)	0.716
Current PCP (Yes)	34 (100.0)	30 (93.8)	31 (93.9)	33 (94.3)	0.542
Current Endocrinologist (Yes)	11 (32.4)	7 (21.9)	8 (24.2)	8 (22.9)	0.748

### Results: Odds Ratio for Depression Diagnosis at Post-Treatment

Outcome	Odds Ratio (95% CI)			P Value comparison to USUAL CARE		
	CBT	CBT+EXERCISE	EXERCISE	CBT	CBT+EXERCISE	EXERCISE
Model 1: Full/Partial Remission MDD	12.4 (1.3, 116.7)	2.3 (0.6, 8.5)	5.8 (1.3, 25.8)	0.028	0.218	0.021
Model 2: Full Remission MDD	5.0 (1.4, 18.0)	5.9 (1.7, 20.6)	6.8 (2.0, 22.6)	0.014	0.006	0.002

Logistic regression analysis. Reference group: Usual Care. Treatment group comparisons were adjusted for baseline education status and change in antidepressant or neuropathic pain medications (0 if no change, 1 if an increase) at POST assessment.

### Results: Change in Psychological Outcomes

Outcome	Treatment, Least Square Mean (SE)				P Value comparison to USUAL CARE		
	CBT	CBT+EXERCISE	EXERCISE	USUAL CARE	CBT	CBT+EXERCISE	EXERCISE
	(N=24)	(N=25)	(N=30)	(N=28)			
Beck Depression Inventory	-15.2 (2.0)	-18.1 (1.8)	-14.1 (1.9)	-8.2 (1.9)	0.011	<.001	0.021
Automatic Thoughts Questionnaire	-11.6 (2.6)	-12.0 (2.5)	-12.6 (2.7)	-2.8 (2.6)	0.018	0.010	0.006
Diabetes-Related Distress	-0.7 (0.2)	-0.6 (0.2)	-0.7 (0.2)	0.1 (0.2)	0.003	0.008	0.001
Exercise Self-Efficacy	-3.2 (3.3)	9.6 (3.2)	6.5 (3.5)	-7.8 (3.3)	0.329	<.001	0.002
SF-12							
PCS	-2.1 (1.7)	1.8 (1.6)	-1.1 (1.7)	-5.5 (1.6)	0.147	0.001	0.047
MCS	12.9 (2.5)	10.1 (2.4)	11.8 (2.6)	6.3 (2.5)	0.069	0.270	0.109
Diabetes Quality of Life	6.8 (2.1)	12.2 (2.1)	10.8 (2.2)	0.9 (2.3)	0.061	<.001	0.001

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Diabetes Quality of Life	6.8 (2.1)	12.2 (2.1)	10.8 (2.2)	0.9 (2.3)	0.061	<.001	0.001

### Results: Medical Outcomes at Post-Treatment

Outcome <sup>1</sup>	Treatment, Least Square Mean (SE)				P Value comparison to USUAL CARE		
	CBT (N=24)	CBT+EXERCISE (N=25)	EXERCISE (N=30)	USUAL CARE (N=28)	CBT	CBT+EXERCISE	EXERCISE
HbA1c							
(N=16)	(N=10)	(N=18)	(N=16)				
-0.31 (0.48)	-1.30 (0.53)	-0.65 (0.47)	0.54 (0.39)	0.526	<.0192	0.178	
Fasting Glucose	10.6 (10.9)	-23.2 (10.5)	-4.7 (10.9)	1.7 (10.7)	0.562	0.091	0.653
Total Cholesterol	-4.4 (6.3)	-4.2 (5.9)	-5.0 (6.2)	13.2 (6.1)	0.038	0.052	0.037
High Density Lipoprotein	-0.5 (1.4)	1.2 (1.4)	-1.0 (1.4)	0.4 (1.4)	0.677	0.654	0.471
Low Density Lipoprotein	-6.2 (4.9)	-2.1 (4.6)	0.1 (4.8)	1.8 (4.7)	0.241	0.541	0.780
Triglycerides	-1.6 (13.6)	-20.1 (12.9)	-8.6 (13.5)	10.4 (13.8)	0.538	0.099	0.293
BMI	0.6 (0.5)	0.04 (0.5)	0.1 (0.5)	0.9 (0.5)	0.646	0.183	0.218
6 Minute Walk Test Distance (ft)	-6.2 (33.0)	0.7 (31.5)	65.6 (32.6)	23.7 (33.3)	0.529	0.605	0.329

1. Treatment group comparisons for non-A1c outcomes were adjusted for baseline education status and baseline outcome values.  
2. Treatment group comparisons for A1c were adjusted for baseline education status, baseline outcome values, and change in diabetes medication (0 if no change, 1 if an increase, -1 if a decrease) at POST Assessment.


## Summary



- Cognitive Behavioral Therapy, Exercise and Combination interventions
  - **significantly improved** depression diagnosis and depressive symptom outcomes.
- Cognitive Behavioral Therapy + Exercise intervention
  - **significantly improved** A1c values by 1.30% (for those with elevated baseline values) compared to Usual Care
- Improvements observed in:
  - Diabetes-related distress
  - Quality of life
- Program ACTIVE tools are:
  - effective and extend access to depression care in rural and urban underserved areas.

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## Collaborators



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## Acknowledgements




Research reported in this presentation was supported by the National Institute Of Diabetes And Digestive And Kidney Diseases of the National Institutes of Health under Award Number R18DK092765.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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## Acknowledgements: Community Partners

## Thank You!

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