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

Mary de Groot, Ph.D.
W. Guyton Hornsby, Jr., Ph.D.
Chandan Saha, Ph.D.
Ziyi Yang, M.S.
Yegan Pillay, Ph.D.
Karen Mathur, M.D.
Jay H. Shubrook, D.O.

**Disclosure to Participants**

- Notice of Requirements For Successful Completion
  - Please refer to learning goals and objectives
  - Learners must attend the full activity and complete the evaluation in order to claim continuing education credit/hours
- Conflict of Interest (COI) and Financial Relationship Disclosures:
  - Mary de Groot, Ph.D. – Faculty, Johnson & Johnson Diabetes Institute, Inc.
  - W. Guyton Hornsby, Jr., Ph.D. – No COI/Financial Relationship to disclose
  - Chandan Saha, Ph.D. – No COI/Financial Relationship to disclose
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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; Nefset 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 (Krogh et al., J Clin Psychiatry, 2009)
  - 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
  - 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 (Buscemi, et al.; Kemeny, et al., 2005)
- VA Walking Study (Buscemi, et al.; Kemeny, et al., 2005)
  - 251 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
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.

Study Aims

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)

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

Eligibility Criteria

- Inclusion criteria:
  - Age 21 or older
  - Diagnosis of type 2 diabetes (duration ≥ 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

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, axenesis 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
### Results: Baseline Demographics

| Outcome                        | CBT (N=25) | CBT+EXERCISE (N=30) | EXERCISE (N=30) | USUAL CARE (N=28) | CBT    | CBT+EXERCISE | EXERCISE | USUAL CARE | P Value  
|--------------------------------|------------|---------------------|-----------------|-------------------|--------|--------------|----------|------------|----------
| Age in years, Mean (SD)        | 57.9 (10.9) | 57.1 (10.7)         | 54.6 (10.7)     | 54.2 (10.4)       |        |              |          |            | 0.367    
| Marital Status                 |            |                     |                 |                   |        |              |          |            |          
| 1: Never Married               | 3 (12.0%)  | 4 (13.3%)           | 4 (13.3%)       | 5 (17.9%)         |        |              |          |            |          
| 2: Married                     | 19 (76.0%) | 14 (46.7%)          | 20 (66.7%)      | 20 (71.4%)        |        |              |          |            |          
| 3: Divorced                    | 2 (8.0%)   | 2 (6.7%)            | 2 (6.7%)        | 3 (10.7%)         |        |              |          |            |          
| 4: Separated/ Widowed          | 2 (8.0%)   | 2 (6.7%)            | 2 (6.7%)        | 2 (7.1%)          |        |              |          |            |          
| Education                      |            |                     |                 |                   |        |              |          |            |          
| 1: Less than High School       | 6 (24.0%)  | 5 (16.7%)           | 5 (16.7%)       | 4 (14.3%)         |        |              |          |            |          
| 2: High School                 | 8 (32.0%)  | 14 (46.7%)          | 15 (50.0%)      | 14 (50.0%)        |        |              |          |            |          
| 3: 4-Year College or higher    | 15 (60.0%) | 13 (43.3%)          | 14 (46.7%)      | 20 (71.4%)        |        |              |          |            |          
| 4: Trade School/Part College   | 8 (32.0%)  | 14 (46.7%)          | 15 (50.0%)      | 13 (46.0%)        |        |              |          |            |          
| Income                         |            |                     |                 |                   |        |              |          |            |          
| 1: <$41,000                    | 6 (24.0%)  | 4 (13.3%)           | 8 (26.7%)       | 5 (17.9%)         |        |              |          |            |          
| 2: $41,000 – $60,000           | 14 (56.0%) | 13 (43.3%)          | 10 (33.3%)      | 9 (32.1%)         |        |              |          |            |          
| 3: $21,000 – $40,000           | 15 (60.0%) | 13 (43.3%)          | 14 (46.7%)      | 20 (71.4%)        |        |              |          |            |          
| 4: $61,000 – $80,000           | 8 (32.0%)  | 14 (46.7%)          | 15 (50.0%)      | 13 (46.0%)        |        |              |          |            |          
| Diabetes-Related Distress      |            |                     |                 |                   |        |              |          |            |          
| 1: -.7 (.2)                    | -1.1 (.3)  | -1.1 (.3)           | -1.1 (.3)       | -.8 (.3)          |        |              |          |            |          
| 2: -.6 (.2)                    | -1.1 (.3)  | -1.1 (.3)           | -1.1 (.3)       | -.8 (.3)          |        |              |          |            |          
| 3: -.7 (.2)                    | -1.1 (.3)  | -1.1 (.3)           | -1.1 (.3)       | -.8 (.3)          |        |              |          |            |          

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

| Outcome                          | CBT (N=24) | CBT+EXERCISE (N=34) | EXERCISE (N=30) | USUAL CARE (N=28) | Odds Ratio (95% CI) | P Value  
|----------------------------------|------------|---------------------|-----------------|-------------------|---------------------|----------
| Remission MOD                    | 3.4 (1.7)  | 3.4 (1.7)           | 3.4 (1.7)       | 3.4 (1.7)         | 1.0 (0.6, 1.7)      | .838     
| Remission MOD                    | 3.4 (1.7)  | 3.4 (1.7)           | 3.4 (1.7)       | 3.4 (1.7)         | 1.0 (0.6, 1.7)      | .838     
| Remission MOD                    | 3.4 (1.7)  | 3.4 (1.7)           | 3.4 (1.7)       | 3.4 (1.7)         | 1.0 (0.6, 1.7)      | .838     

### Results: Change in Psychological Outcomes

| Outcome                          | Treatment, Least Square Mean (SE) | P Value comparison to USUAL CARE  
|----------------------------------|-----------------------------------|----------------------------------
| Diabetes Quality of Life         | 6.8 (2.1)                         | .061                             
| Exercise Self-Efficacy           | -3.2 (3.3)                        | .329                             
| Diabetes-Related Distress        | -.7 (0.2)                         | .109                             
| Automatic Thoughts Inventory     | -.7 (0.2)                         | .109                             
| Beck Depression                  | -.7 (0.2)                         | .109                             
| SF-12 PCS                        | -2.1 (1.7)                        | .001                             
| SF-12 MCS                        | 12.9 (2.5)                        | .001                             

### Results: Medical Outcomes at Post-Treatment

| Outcome                          | Treatment, Least Square Mean (SE) | P Value comparison to USUAL CARE  
|----------------------------------|-----------------------------------|----------------------------------
| 6 Minute Walk Test               | 156.7 (18.0)                      | .001                             
| BMI                              | 0.6 (0.5)                         | .183                             
| Triglycerides                    | -1.6 (13.6)                       | .099                             
| Fasting Glucose                  | 10.6 (10.9)                       | .091                             
| Remission MOD                    | 3.4 (1.7)                         | .838                             
| Remission MOD                    | 3.4 (1.7)                         | .838                             
| Remission MOD                    | 3.4 (1.7)                         | .838                             

Notes:
1. Treatment group comparisons for non-A1c outcomes were adjusted for baseline education status and change in diabetes medication. 
2. Treatment group comparisons for non-A1c outcomes were adjusted for baseline education status and change in diabetes medication. 
3. Treatment group comparisons for A1c were adjusted for baseline education status, baseline outcome values, and change in diabetes medication. 
4. Treatment effects were calculated as the change from baseline to 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.

Collaborators

Staff
Barb Myers, B.S., C.C.R.P.  Melinda Ruberg
David Donley, M.S.  Sara Miekims, M.A.
Alex Tyka, M.S.  Daniella Epler, M.A.
Rachel Giff, R.N.  Ellen Knapp, M.A.
Susan Eason, B.S.  Molly Long, M.A.
Jaclyn Bape, M.S.  Michael Craven, M.A.
Kalen Kearcher, M.S.  Amber Massa
Debby Wilmer, M.S.  Alycia Ramirez
Kelly Chaudoin, Psy.D.  Lynn Pietrik, R.N.
Chelsay Holbert, Psy.D.  Cammie Starner, R.N.
Michelle Weinstein, M.A.  Christiaan Abildso, Ph.D.

Referring Physicians
- Indiana: Dr. Carolina Bruno; Dr. Paris Roach; Connie Gilbert, RD; Dr. James Meacham
- Ohio: Dr. Frank Schwartz; Regina Reed, NP; Dr. Jennifer Leavitt; Dr. Steven Richards; Dr. Dinora Armstrong; Dr. Milagros Lopez Velez; Dr. Hitshbagdagi Kupadev; Dr. Leah Hopkins; Dr. Geetha Conjeevaram; Dr. Tanil Cools; Dr. Aki Gao; Dr. Kimberly Spencer; Dr. Jeremiah Nelson; Dr. Gisegus Bhatnath; Dr. Amber Healy; Dr. Brian Still
- West Virginia: Dr. Clinton Cooper; Dr. Arthur Ward; Dr. Richard Simpson

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Thank You!