Depression, Distress and Diabetes

Mark Peyrot, PhD

Mark.Peyrot@gmail.com

AADE15

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:
  - Presenter: Mark Peyrot, PhD; Astra Zeneca, Calibra, GlaxcoSmithKline, Lilly, Novo Nordisk
- Non-Endorsement of Products:
  - Accredited status does not imply endorsement by AADE, ANCC, ACPE or CDR of any commercial products displayed in conjunction with this educational activity
- Off-Label Use:
  - Participants will be notified by speakers to any product used for a purpose other than for which it was approved by the Food and Drug Administration.

AADE15

Significance of Depression in Diabetes

- Less self-care (inactivity, smoking, etc.)
- Glucose disregulation
- Obesity
- Major predictor of poor outcomes (functional limitations, morbidity, mortality, health care utilization)
- Effect of depression is exacerbated in diabetes

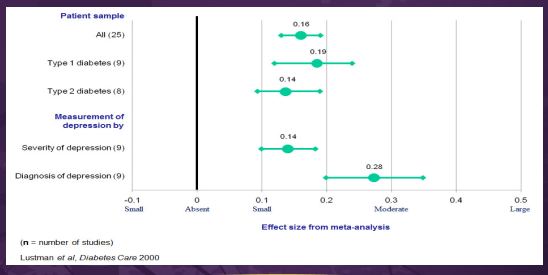
AADE15

Depression is Associated with Non-Adherence to Diabetes Self-Care: Meta-Analysis

	n	z (P)	Weighted r	95% CI
Overall analysis	47	9.81 (<0.001)	0.21	0.17 – 0.25
Appointment keeping	4	21.58 (<0.001)	0.31	0.29 – 0.34
Composite measures	18	9.66 (<0.001)	0.29	0.23 – 0.34
Diet	18	7.60 (<0.001)	0.18	0.13 – 0.22
Medication	18	5.15 (<0.001)	0.14	0.09 – 0.20
Exercise	13	7.89 (<0.001)	0.14	0.10 – 0.17
Glucose monitoring	15	3.50 (<0.001)	0.10	0.04 – 0.16
Foot care	2	0.88 (0.380)	0.07	-0.08 to 0.21

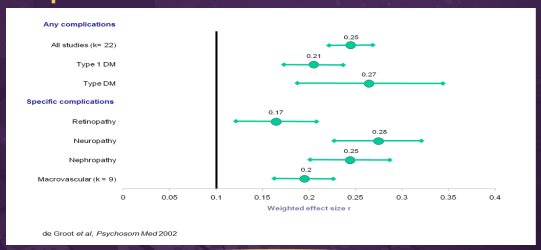
Gonzalez *et al, Diabetes Care* 2008

Depression is Associated with Hyperglycaemia



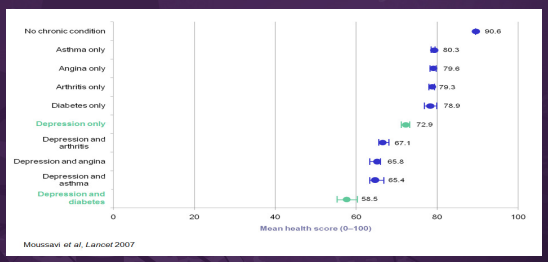
Lustman *et al, Diabetes Care* 2000

Depression is Associated with Diabetes Complications



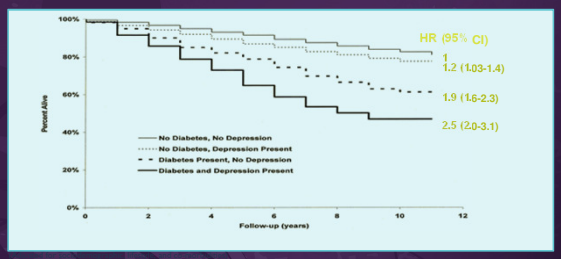
de Groot *et al, Psychosom Med* 2002

Depression-Diabetes Co-Morbidity is Associated with Worst Health



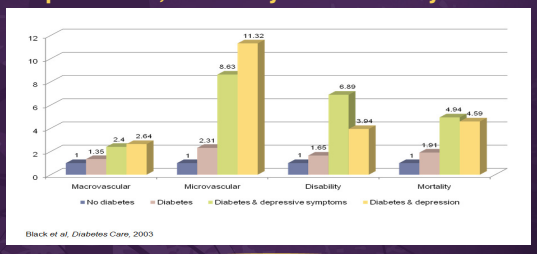
Moussavi *et al, Lancet* 2007

Depression and Diabetes Co-Morbidity is Associated with Mortality



Egede *et al, Diabetes Care 2005*

Even Subclinical Depression Increases Complications, Disability and Mortality



Black *et al, Diabetes Care*, 2003

Diabetes-related Distress

- DRD is not depression, but is associated with having symptoms of depression
- DRD is a direct reflection of the burden of diabetes, the subjective experience of that burden
- DRD can impair self-care and is more strongly associated with diabetes outcomes than is depression

AADE15

Diagnosed Depression vs Depression Symptoms and Diabetes-specific Distress

- Type 2 DM patients assessed for major depressive disorder (MDD), self-report depressive symptoms, and diabetes-specific distress
- 70% of patients with elevated depressive symptoms did not meet criteria for MDD and 34% of MDD patients did not report increases in depressive symptoms
- Elevated depressive symptoms (generalized distress) more reflective of diabetes-related distress than of MDD
- Elevated levels of depressive symptoms and not MDD were significantly associated with biological (HbA1c) and behavioural (diet; exercise) health indicators

AADE15

Fisher *et al, Diabetes Care* 2007

Prevalence of Depression in Diabetes

- US estimates of prevalence are 15-40% (2-8 times the general population)
- The wide range in estimates is a result of methodological differences in studies
- Consistent finding of higher rates in diabetes

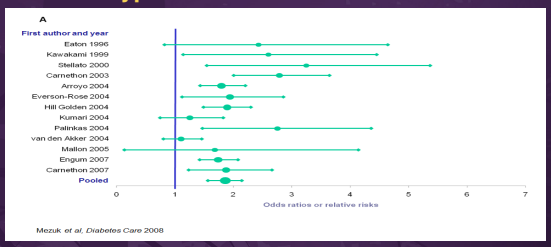
AADE15

Diabetes & Depression: Chicken or Egg?

- Does diabetes cause depression or does depression cause diabetes?
- Evidence for both causal mechanisms
  - Burden of diabetes is stressful/distressing
  - Depression increases risk for diabetes (even when controlling for behavior, weight)
- Some have suggested depression is another element of the metabolic syndrome

AADE15

Baseline Depression Predicts Incident Type 2 Diabetes



Mezuk *et al, Diabetes Care* 2008

Depression and Diabetes Risk

- Seminal studies done at Johns Hopkins
  - Eaton et al identified phenomenon
  - Golden et al found depression a predictor of diabetes but effect mediated by lifestyle factors
- Rubin, Peyrot et al studied association between depression and diabetes risk in the Diabetes Prevention Program (DPP)

AADE15

Assessing Depression in DPP

- Disabling depression or high ADM use = exclusion
- No depression diagnosis available
- Beck Depression Inventory (BDI) assessed every 6 months
- Anti-depression medication (ADM) assessed each year (medication review)
- More ADM than high BDI (low elevation of BDI used in analyses), little overlap in markers

(*Diabetes Care* 2008;31:420–426)

AADE15

Depression as a Risk Factor

- Elevated BDI scores at baseline or during the study were not associated with diabetes risk in any arm
- Baseline ADM use was associated with diabetes risk in the Placebo and Intensive Lifestyle arms
- ADM use during the study (compared with no use) was also associated with diabetes risk in the Placebo and Intensive Lifestyle arms
- The association persisted when controlling for weight level/gain

AADE15

Possible Interpretations

- Antidepressant use could simply be a marker for the actual cause(s) of increased diabetes risk, which may be more severe, chronic, or recurrent depression
- Antidepressant medication may have diabetogenic physiological effects

AADE15

Biomedical Perspectives

- Depression may be part of a metabolic syndrome that includes diabetes and CVD
  - Result of stress hormones and/or inflammation
- Depression may be a psychological complication of diabetes and/or complications of diabetes
- If the former, depression in undiagnosed and diagnosed diabetes would be equally high

AADE15

Meta-analysis Findings

(*Diabetes Care* 2011;34:752–762)

- Risk for depression not increased in impaired (IGM) vs normal (NGM) glucose metabolism
- Risk for depression did not differ between individuals with undiagnosed DM and individuals with either NGM or IGM
- Risk of depression was significantly lower for individuals with IGM or undiagnosed DM relative to those with diagnosed DM

AADE15

Implications

- Depression does not seem to be a result of metabolic dysfunction, b/c it is not elevated in those with undiagnosed diabetes or IGM relative to those with normal glucose
- Depression is elevated in those with diagnosed diabetes relative to those with undiagnosed diabetes or IGM, suggesting that it is due to increased psychosocial burden of illness

AADE15

Risks of High Depression Symptomatology

Category	Odds Ratio (95%CI)
Female (vs. male)	2.29 (1.58-3.87)
Not married (vs married)	1.55 (1.07-2.25)
Education = High school*	1.90 (1.23-2.92)
Education < High school*	2.64 (1.52-4.57)
Complications = 3-4**	1.90 (1.10-3.28)
Complicaions = 5-9**	3.29 (1.62-6.66)

* Compared to Education > High school

** Compared to Complications = 0-2 (9 possible)

M. Peyrot and R. Rubin, *Diabetes Care*, 20, 1997

AADE15

Rates of High Depression Symptomatology

Probabilities for risk categories:

If no risk factors, synthetic probability = 5%

Actual probability for lowest risk case = 10%

If all risk factors, synthetic probability = 92%

Actual probability for highest risk case = 81%

M. Peyrot and R. Rubin, *Diabetes Care*, 20, 1997

AADE15

Psychological Correlates of Depression

Diabetes-Specific

- Fantasy coping (+)
- Tx self-efficacy (-)
- Illness burden (?)

Generic

- Anger coping (+)
- Self-esteem (-)
- Stress (+)

AADE15

Mediated Relationships

- Age mediated by: spouse (+), complications (+), anger (-), global & diabetes efficacy (-), stress (-)
- Gender (female) mediated by: spouse (-), education (-), complications (-), global & diabetes efficacy (-), stress (+)
- Education mediated by: fantasy (-), global & diabetes efficacy (+)
- Complications mediated by: anger (+), fantasy (+), global & diabetes efficacy (-), stress (+)

Direction of relationship in parentheses

AADE15

Synergistic Relationships

- Interactions with gender
  - Global efficacy stronger for men (-)
  - Diabetes efficacy stronger for women (-)
  - Fantasy coping stronger for women (+)
- Interactions significant for men only
  - Stress X Anger (+)
  - Stress X Diabetes efficacy (-)
  - Complications X Fantasy (+)
  - Complications X Diabetes efficacy (+)

Direction of relationship in parentheses

AADE15

Persistence of Depression

- 42% of participants in diabetes education were depressed at start of 5-day program
- 13% were depressed when program started, and ended, and 6 months later
  - If depressed only at pre or post program (not both), 36% were depressed at 6 months
  - If depressed at both pre and post program, 73% were depressed at 6 months

M. Peyrot and R. Rubin, *Diabetes Care*, 22, 1999

AADE15

Distress and Psychiatric Dx

- If possible, start with interventions that can be implemented during regular visits before considering more intensive interventions which may require referral to a behavioral/psychosocial specialist
- If symptoms are too severe, the provider should move directly to referral to or consultation with a specialist

AADE15

Action Steps for Treating Distress and Psychiatric Dx

1. Identify patients who are suffering from diabetes-related distress
2. Apply effective treatments to relieve diabetes-related distress
3. Identify patients who are suffering from psychiatric disorders
4. Refer patients for specialized mental health care when appropriate

Peyrot et al, Diabetes Care 2007

AADE15

Identifying Diabetes Distress

- If patient is unwilling or unable to engage in active self-management despite recognizing a need for change
- Distressed patients can be identified by asking them questions designed to assess specific sources of distress as well as the intensity of this distress:
  - Are you having trouble accepting your diabetes?
  - Do you feel overwhelmed or burned out by the demands of diabetes management?
  - Do you get the support you need from your family for diabetes management?

AADE15

Alleviating Diabetes Distress

- Strategies
  - Enhance diabetes-specific self-efficacy
  - Encourage realistic expectations
  - Enhance motivation
- Techniques
  - Psycho-educational (coping skills training)
  - Motivational Interviewing

AADE15

Under-Diagnosis of Depression in Diabetes

- Depression is recognized in only about one-third of cases where it exists
- Under-diagnosis reflects the assumption that depression is secondary to diabetes (not independently important)
- Under-diagnosis is a result of lack of training and time for diagnosis and treatment

AADE15

Identifying Clinical Depression

- Patients likely to be clinically depressed can be identified by asking two questions about the DSM-IV cardinal diagnostic criteria:
  - "During the past 2 weeks, have you felt down, depressed, or hopeless?" and
  - "During the past 2 weeks, have you lost interest or pleasure in doing things?"
- Positive responses to one or both questions should trigger questions about the remaining 7 DSM-IV symptoms.

AADE15

Secondary Criteria for Diagnosis

- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue
- Significant weight loss or gain
- Feeling worthless or guilty
- Difficulty concentrating or making decisions
- Recurrent thoughts of death or suicide

AADE15

Symptom Characteristics

- Symptoms present most of day
- Symptoms present for $\geq$ 2 weeks
- Symptoms cause distress, impairment
- Symptoms not attributable to medications, medical condition, bereavement

AADE15

Screening Tools

- Center for Epidemiological Studies Depression Scale (CESD)
- Beck Depression Inventory (BDI)
- Patient Health Questionnaire (PHQ-9)
- Tools for screening, not diagnosis
- Re-screen (2-4 weeks) if above cut-off (but if suicidal treat or refer immediately)
- Treat or refer if above cut-off twice

AADE15

Signs of Depression in Medical History

- Medical history of depression, anxiety disorder, substance abuse, mental health treatment
- Family history of depression
- Persistent focus on somatic complaints, especially pain, without organic basis
- Sexual dysfunction

AADE15

Treating Psychiatric Disorders

- Medication and behavioral therapy can be effective, separately or combined
- Counseling (eg, CBT, CST) is indicated for treatment of psychiatric disorders in diabetes, even if medication is used
- Some disorders (anorexia, substance abuse, depression with suicidal ideation) may require residential treatment

AADE15

Pharmacological Therapy for Depression in Diabetes

- Tricyclics are effective
- SSRIs are effective
- Side-effects of antidepressant medications

AADE15

Behavioral Therapy for Depression in Diabetes

- Cognitive behavioral therapy (CBT) is effective
- Psycho-educational treatment (CST) may be effective, especially if
  - Depression is diabetes-driven
  - Depression is subclinical

AADE15

Effects of Depression Treatment in Diabetes

- Remission of depression may be associated with improved glycemic control
- Behavioral therapy is more likely to result in improved glycemic control
- But improved glycemic control is not sufficient for depression remission

AADE15

RCTs Show Effects of Depression Treatment on Mood and Glycemia

Reference	n	Interventions	Intervention superior to control group?	
			Psychological Outcome	Medical Outcome
Pharmacological treatments (4 RCTs, n=289)				
Lustman, 1997	28	Nortriptiline vs placebo	Yes	No
Lustman, 2000	60	Fluoxetine vs Placebo	Yes	No
Lustman, 2006	152	Sertraline vs placebo	Yes	No
Pulk-Hyvarinen, 2007	49	Paroxetine vs placebo	No	No
Psychological treatments (3 RCTs, n=140)				
Lustman, 1988	51	CBT+education vs education	Yes	Yes
Huang, 2001	59	Group counselling vs usual	Yes	Yes
Simson, 2008	30	Supportive psychotherapy vs usual	Yes	No
Mixed treatments (4 RCTs, n=950)				
Williams, 2004	417	Depression management vs usual	Yes	No
Katon, 2004	329	Algorithm-based vs usual	Yes	No
Stiefel, 2008	85	Psychiatric vs usual	Yes	No
Bogner, 2007	123	Algorithm-based vs usual	not specified	Yes

Petrak & Herpertz, *Curr Op Psych* 2009

Realistic Treatment Goals

- Depression (best-studied condition) generally is not curable in patients with diabetes
  - Less than 10% who achieve remission remain depression-free for 5 years
  - Episodes occur about once a year for lifetime
  - Episodes are longer, more severe in diabetes

AADE15

Diabetes and Distress/Depression: Summary

- Potentially devastating combination, even if diabetes control is good
- High prevalence
- Often not diagnosed
- Easily detectable with simple screening tools
- Depression requires specific anti-depressant therapy

AADE15

Diabetes and Distress/Depression: Conclusions

- Routinely screen for distress among people with diabetes
- Counsel all patients with diabetes-related distress
- Treat or refer all patients with depression

AADE15

Diabetes and Distress/Depression: Implications

- Providers should enhance their skills for detecting distress/depression in their patients
- Providers should enhance their skills for treating distress/depression in their patients
- Providers should develop a referral network including specialists in the diagnosis and treatment of depression in patients with diabetes

AADE15

Putting it into Practice

- What would you like to change about your strategies for dealing with distress/depression?
- What has worked for you in the past?
- What is your plan?
- How will you know you are successful?
- How will you reward yourself?

AADE15

References

Black et al, Diabetes Care, 26, 2003
de Groot et al, Psychosom Med 2002
Egede et al, Diabetes Care, 28, 2005
Fisher et al, Diabetes Care, 30, 2007
Gonzalez et al, Diabetes Care, 31, 2008
Lustman et al, Diabetes Care, 21, 2000
Mezuk et al, Diabetes Care, 31, 2008
Moussavi et al, Lancet, 370, 2007
Nouwen et al, Diabetes Care, 34, 2011
Petrak et al, Curr Op Psych, 20, 2009
Peyrot et al, Diabetes Care, 20, 1997
Peyrot et al, Diabetes Care, 22, 1999
Peyrot et al, Diabetes Care, 30, 2007
Rubin et al, Diabetes Care, 31, 2008

AADE15