

Depression, Diabetes, and Cardiovascular Disease

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Disclosure of Interests

- *Research Support*

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- *Consulting Relationships*

None

- *Speaker's Bureau(s)*

None

- *Stock Equity (>\$10,000)*

None

Comorbid Depression and Diabetes

A Case Presentation

- 56-year old white female with T2DM x 6 yrs; poorly controlled on diet and oral agents
- PMHx: obesity, hypertension, CHD with myocardial infarction 1 yr ago
- Called after hearing an ad about a study of depression in persons with diabetes

Comorbid Depression and Diabetes

A Case Presentation

- Presents with untreated MDD, BDI =32, no SI/HI
- First episode age 26 resolved after 1 yr without treatment, ~10 episodes in the last 20 years, longest lasting 2 years
- 2 yrs ago, placed on sertraline by PCP; she stopped after 2 weeks because of headaches

Diabetes Type

- *Type 1 diabetes*

An autoimmune disease that destroys insulin-producing pancreatic cells and leads to insulin deficiency with hyperglycemia. 5-10% of diabetes cases are type 1; most present before adulthood.

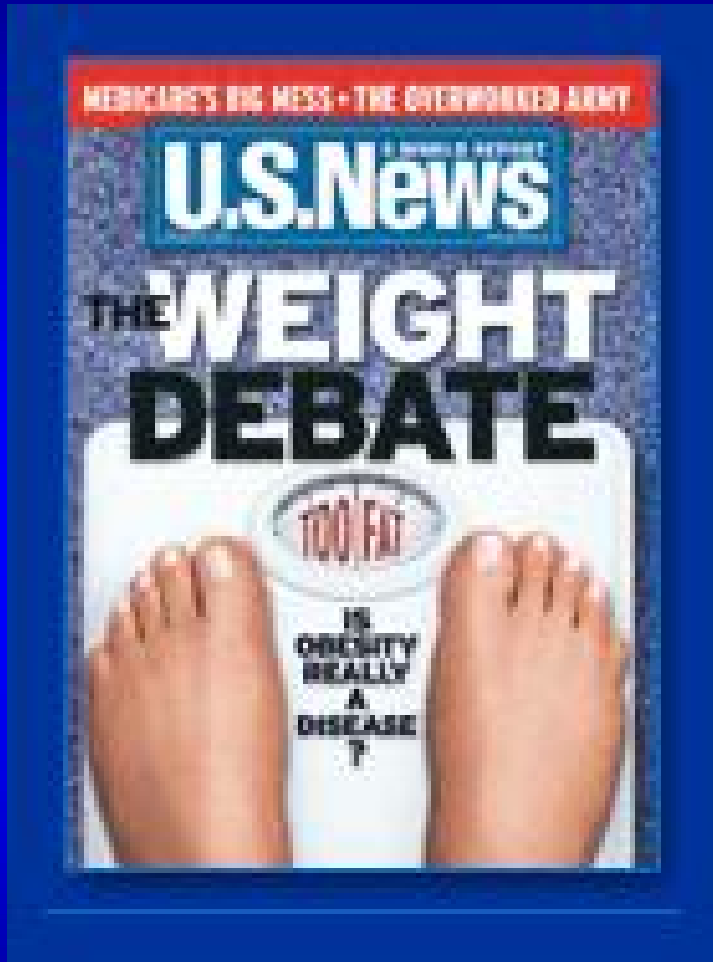
- *Type 2 diabetes*

Results from insulin resistance (a condition in which the body fails to properly use insulin), combined with relative insulin deficiency. 90-95% of diabetes cases are type 2; most present during adulthood.

Prevalence (%) of Diabetes in the US

Prevalence	%	million
<i>Overt Diabetes</i>		
Diagnosed Diabetes	5.9	11.8
Undiagnosed Diabetes	2.4	4.9
Total Overt Diabetes	8.3	16.7
<i>Prediabetes (age ≥20 yrs)</i>		
Impaired Fasting Glucose	6.1	12.3
Impaired Glucose Tolerance	2.5	4.4
Total Prediabetes	8.6	16.7
<i>Total Overt or Prediabetes</i>	16.9	33.4

Fat and Getting Fatter



February 9, 2004

“A majority of Americans
-- now 64% --
are overweight or obese.”

Age-Adjusted Prevalence of Obesity (Adults 20-74 Years)

	NHANES III 1988-1994 (n=14,468)	NHANES 1999-2000 (n=3,601)
Both	23.3	30.9
Men	20.6	27.7
Women	25.9	34.0

Atherosclerosis and Coronary Heart Disease (CHD) in Diabetes

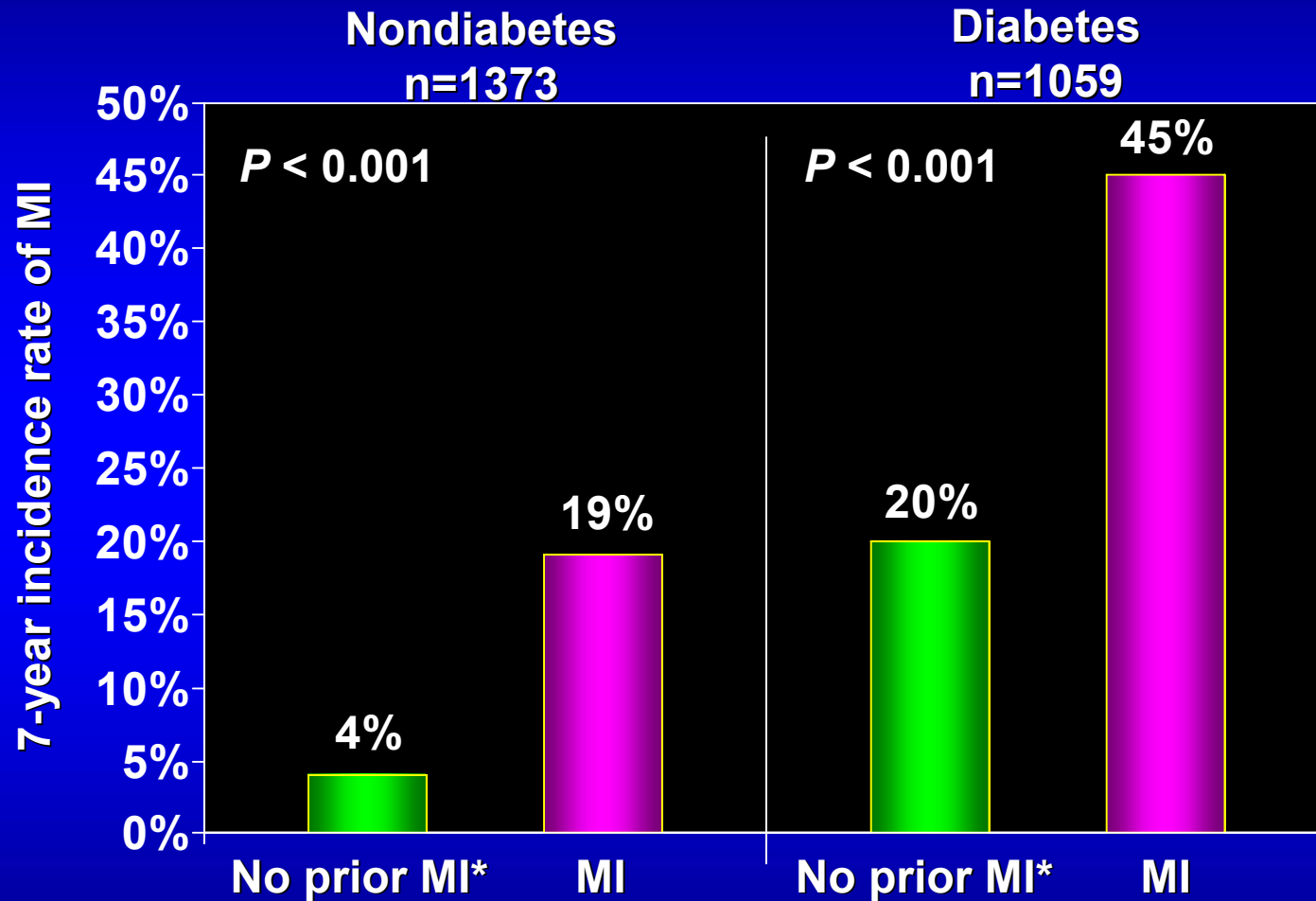
Diabetes:

- Is a powerful independent risk factor for CHD
- increases the risk for CHD 2-4 times over the general population.

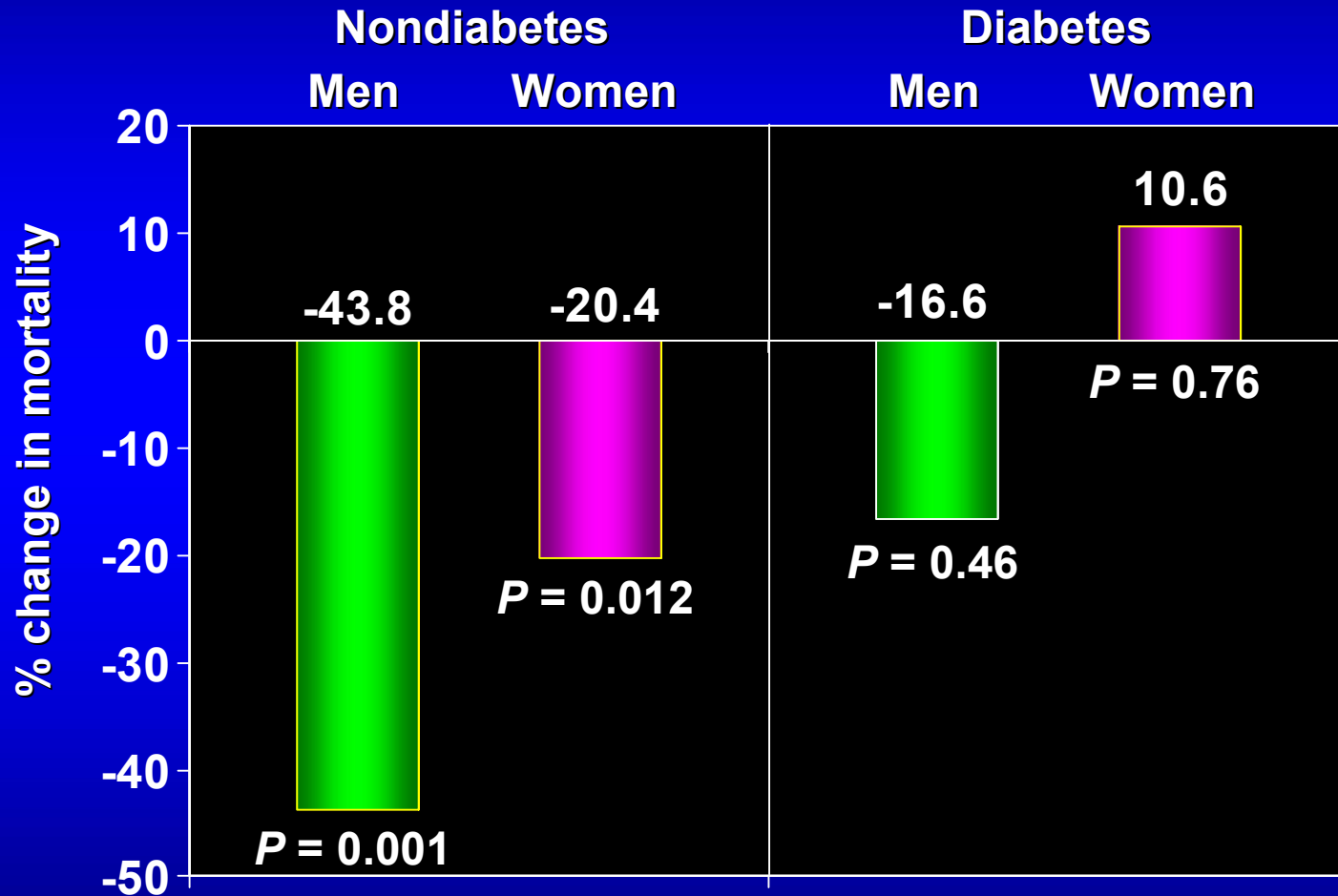
Atherosclerosis accounts for:

- 80% of all deaths in diabetes (50% from CHD).
- 75% of all hospitalizations for diabetic complications.

Type 2 Diabetes and CHD: 7-Year Incidence of Fatal/Nonfatal MI



Changes in CAD Mortality Rates in Patients with and without Diabetes*



*NHANES I (1971-1975) and NHANES II (1982-84)
Gu et al., *JAMA* 1999; 281:1291-1297

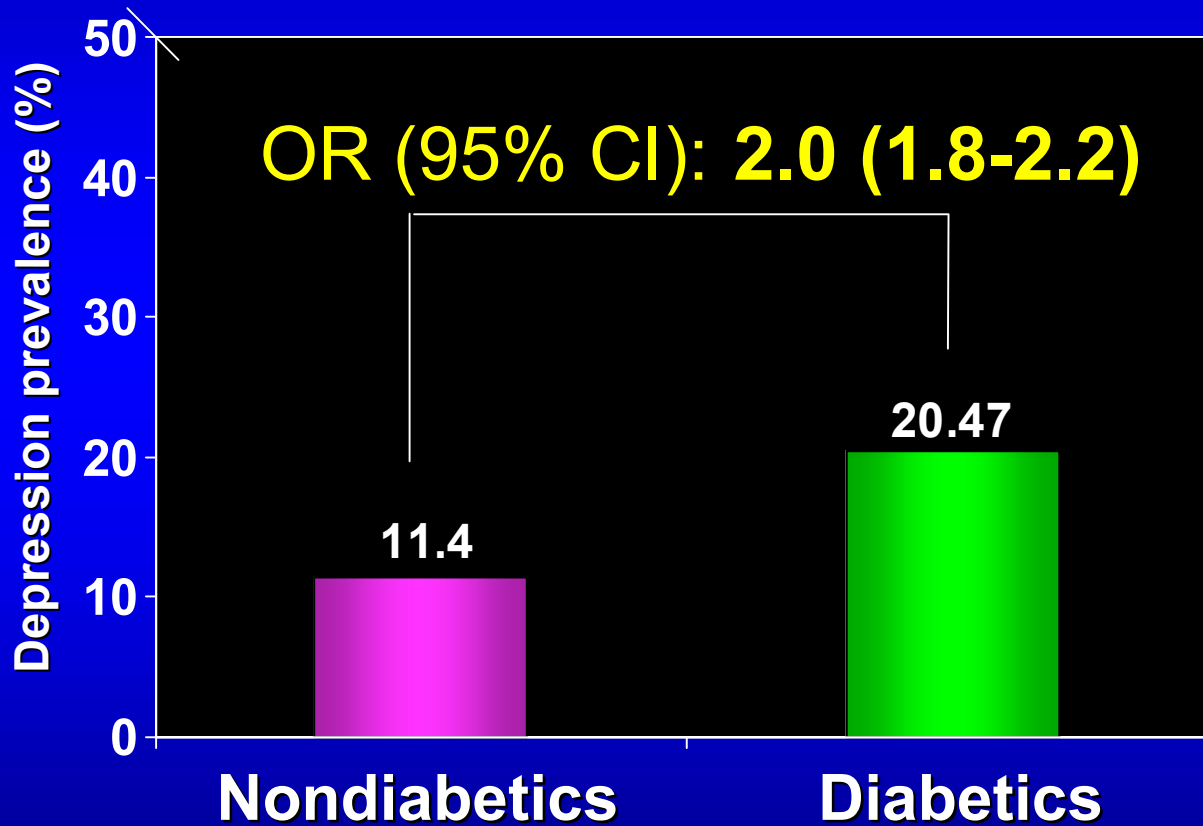
Prevalence (%) of Depression in Persons with and without Diabetes

Prevalence	%	(Millions)
<i>General Population*</i>		
12-month	6.6	13.3
Lifetime	16.2	32.6
<i>Diabetes (16.7 Million)**</i>		
Current	11.0	1.8
Lifetime	28.6	4.8
Elevated symptoms	31.0	5.2

**Kessler (NCS-R 2003)*

***Anderson et al, 2001*

Odds and Prevalence of Depression in 18 Controlled Studies



The odds of depression were doubled in diabetics compared to controls.

Depression Doubles the Risk of T2DM

Study	Follow-up Interval	Incidence T2DM	Covariates	Depression Measure	OR (95% CI)
<i>Eaton '96</i> (ECA, n=1715) N=1715	13 yrs	5.2%	Demographics, SES, health use comorbidity, weight	Diagnosis per DSM	2.2 (0.9-5.6)
<i>Kawakami '99</i> (Japan, n=2764 ♂)	8 yrs	2.3%	Demographics, BMI, comorbidity activity level, smoking, ETOH	Zung Scale Moderate or severe (≥ 48)	2.3 (1.0-5.2)
<i>Carnethon '03</i> (NHANES, n=6190)	15.6 yrs	7.3%	Diabetes risk factors	GWB Dep Scale	1.8 (1.1-2.9)
<i>Golden et al '04</i> (ARIC, n=11,615)	6 yrs	6.2%	Age, race, sex, education	Vital Exhaustion Scale	1.6 (1.3-2.0)

Risk of T2DM by Quartiles of Depressive Symptoms

<i>Adjusted for:</i>	Quartile of depressive symptoms				<i>P</i>
	1	2	3	4	
Model 1: Age, race, education and sex	1.0	1.2	1.3	1.6	<0.0001
Model 2: Metabolic covariates*	1.0	1.1	1.1	1.4	0.0071
Model 3: Lifestyle covariates†	1.0	1.2	1.1	1.5	0.0005
Model 4: Lifestyle covariates and BMI‡	1.0	1.2	1.0	1.3	0.06
Model 5: Metabolic and lifestyle covariates§	1.0	1.1	1.0	1.3	0.04

*Model 2: adjusted for Model 1 + fasting insulin, fasting glucose, log triglycerides, HDL cholesterol, BMI, waist-to-hip ratio, and systolic blood pressure.

†Model 3: adjusted for Model 1 + physical activity, total caloric intake, and smoking status.

‡Model 4: adjusted for Model 3 + BMI and waist-to-hip ratio.

§Model 5: adjusted for Model 2 + Model 3.

|| $P < 0.05$

Association of Depression with Diabetes Complications

Any Complications

All Studies (k=22)

Type 1 DM

Type 2 DM

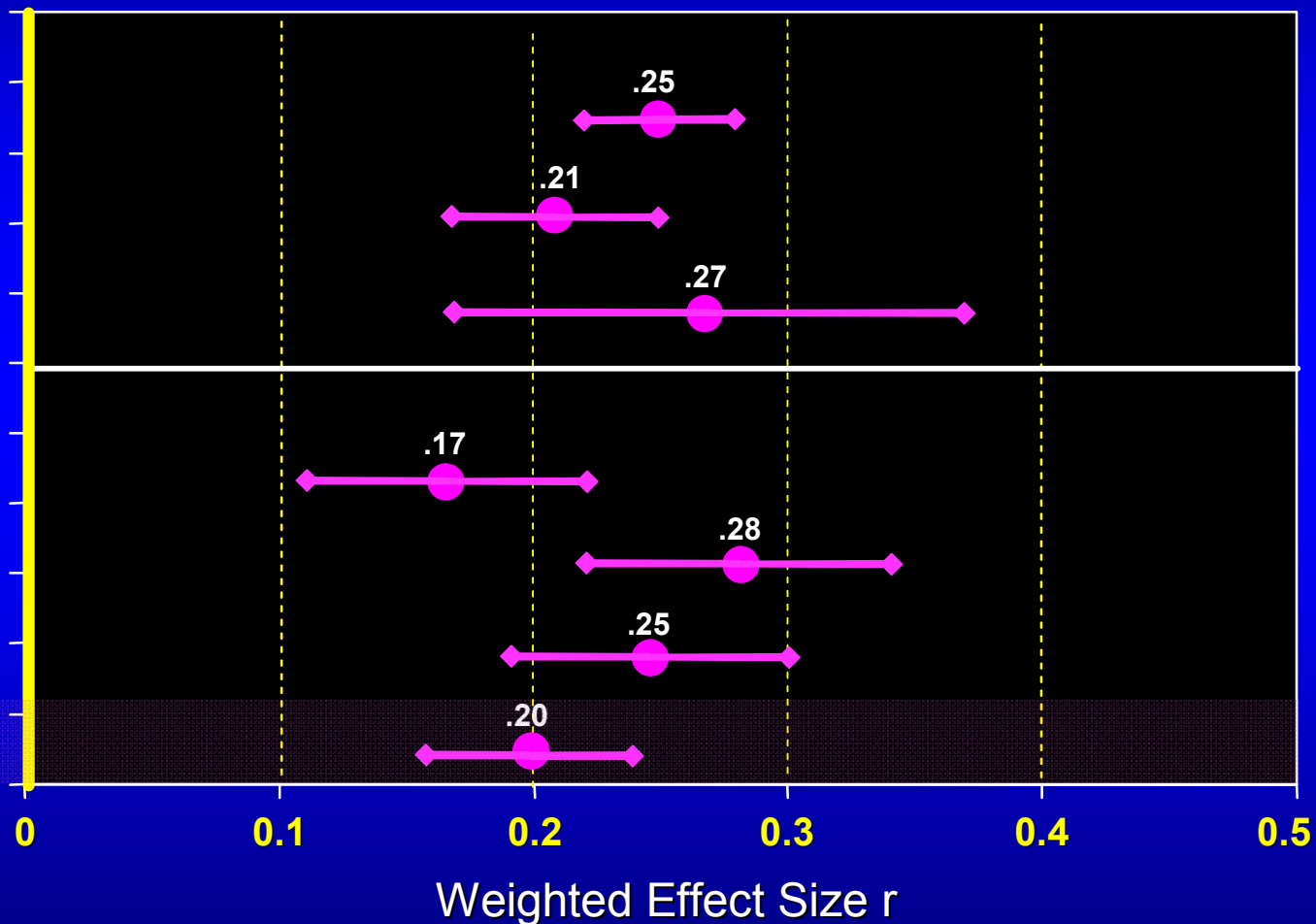
Specific Complications

Retinopathy

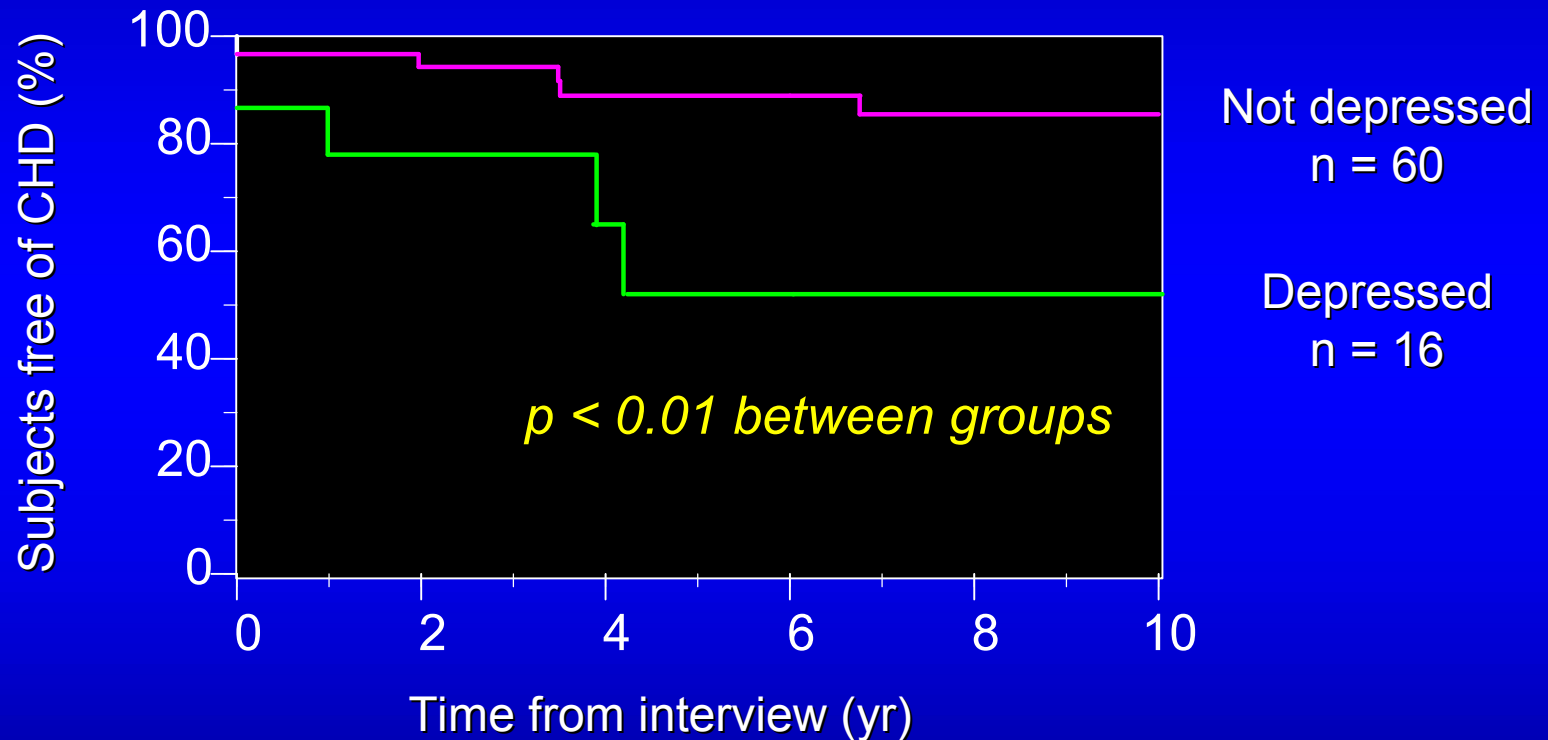
Neuropathy

Nephropathy

Macrovascular (k=9)



Manifest CHD in Relation to Depression: *A 10-yr prospective study in diabetic women*



Age-adjusted hazard ratio 5.2 (1.4-18.9, p = 0.01)

Summary of Epidemiologic Observations

- Depression rates are doubled in the presence of diabetes (both type 1 and type 2).
- Depression occurs in the course of diabetes (primarily type 1).
- Depression increases the risk for diabetes (type 2).
- Depression is more likely in the face of complications (both types).
- Depression predicts morbidity from CHD (both types).

How treatable is depression in a diabetic patient?

Does treatment of depression improve medical outcome?

Comorbid Depression and Diabetes

A Case Presentation

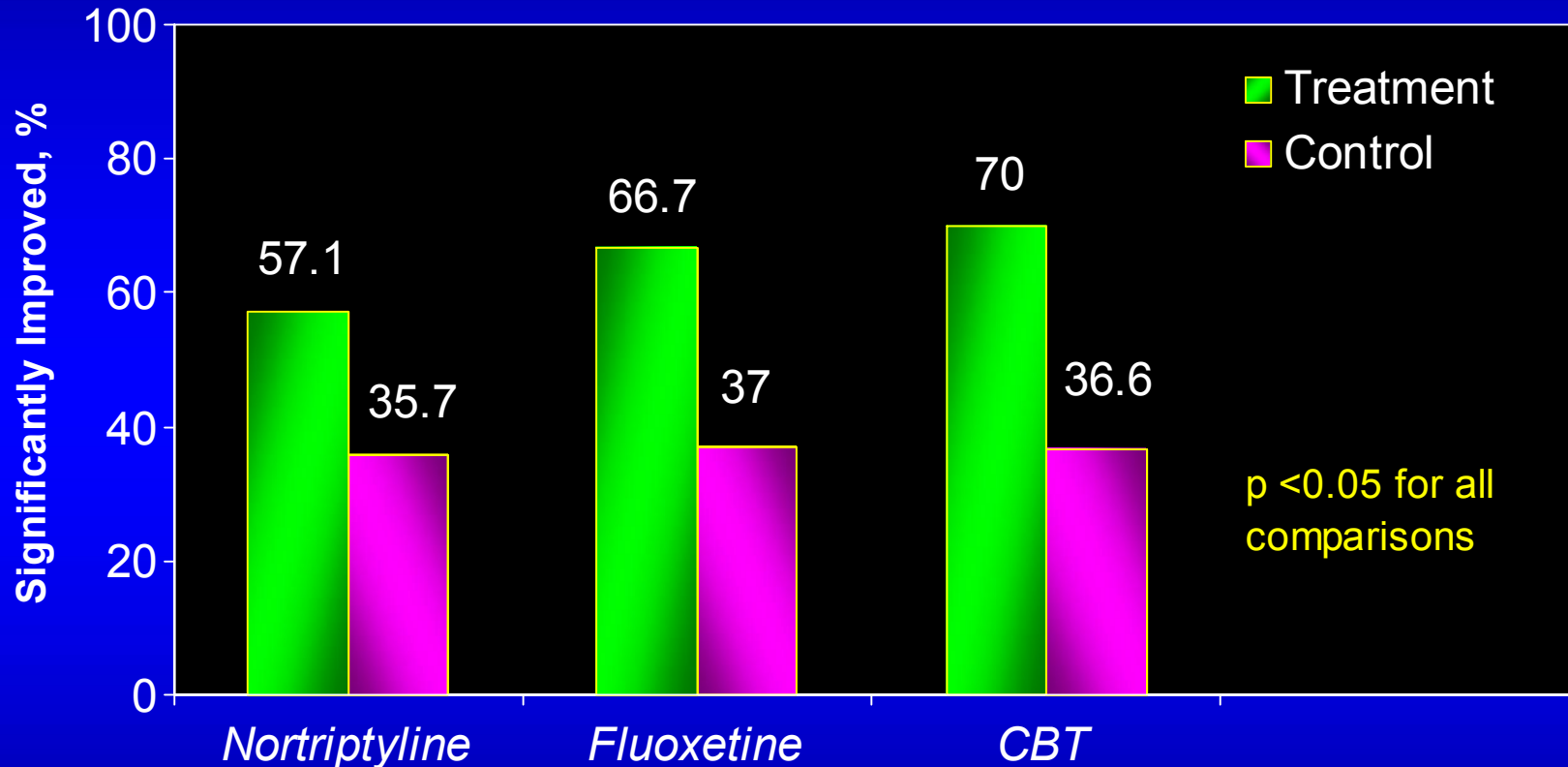
- Entered maintenance trial, started on sertraline in open treatment phase
- Achieved depression remission and mild GHb improvement (-0.2%) on 100 mg/d. Randomly assigned to continue sertraline treatment for 1 year or to recurrence
- Remained depression free over 52 weeks of follow-up; GHb deteriorated to its baseline level

Efficacy of Antidepressant Medication: Meta-analysis of FDA Data Base

Drug	K	N	<i>Mean HAM-D improvement</i>		
			Drug/D	PBO/P	D-P
Fluoxetine	5	1,132	8.3	7.3	1.0
Paroxetine	12	1,289	9.9	6.7	3.2
Sertraline	3	779	10.0	7.9	2.1
Venlafaxine	6	1,148	11.5	8.4	3.1
Nefazodone	8	1,428	10.7	8.9	1.8
Citalapram	4	1,168	9.7	7.7	2.0

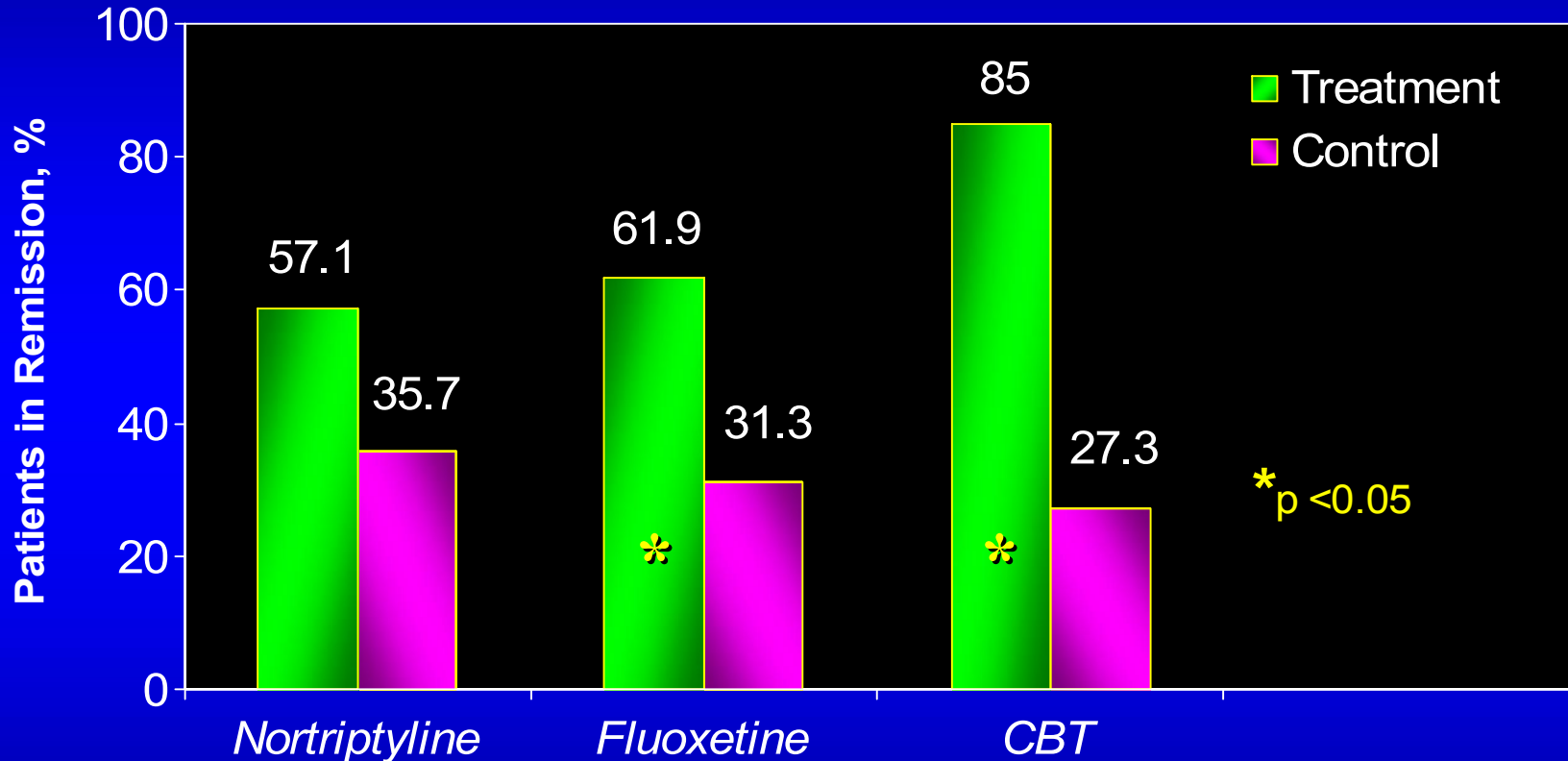
Overall average benefit per HAM-D 2.2

Treatment Effectively Relieves Depression



21.4	29.7	33.4	Treatment – Control (%)
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Treatment Effectively Relieves Depression



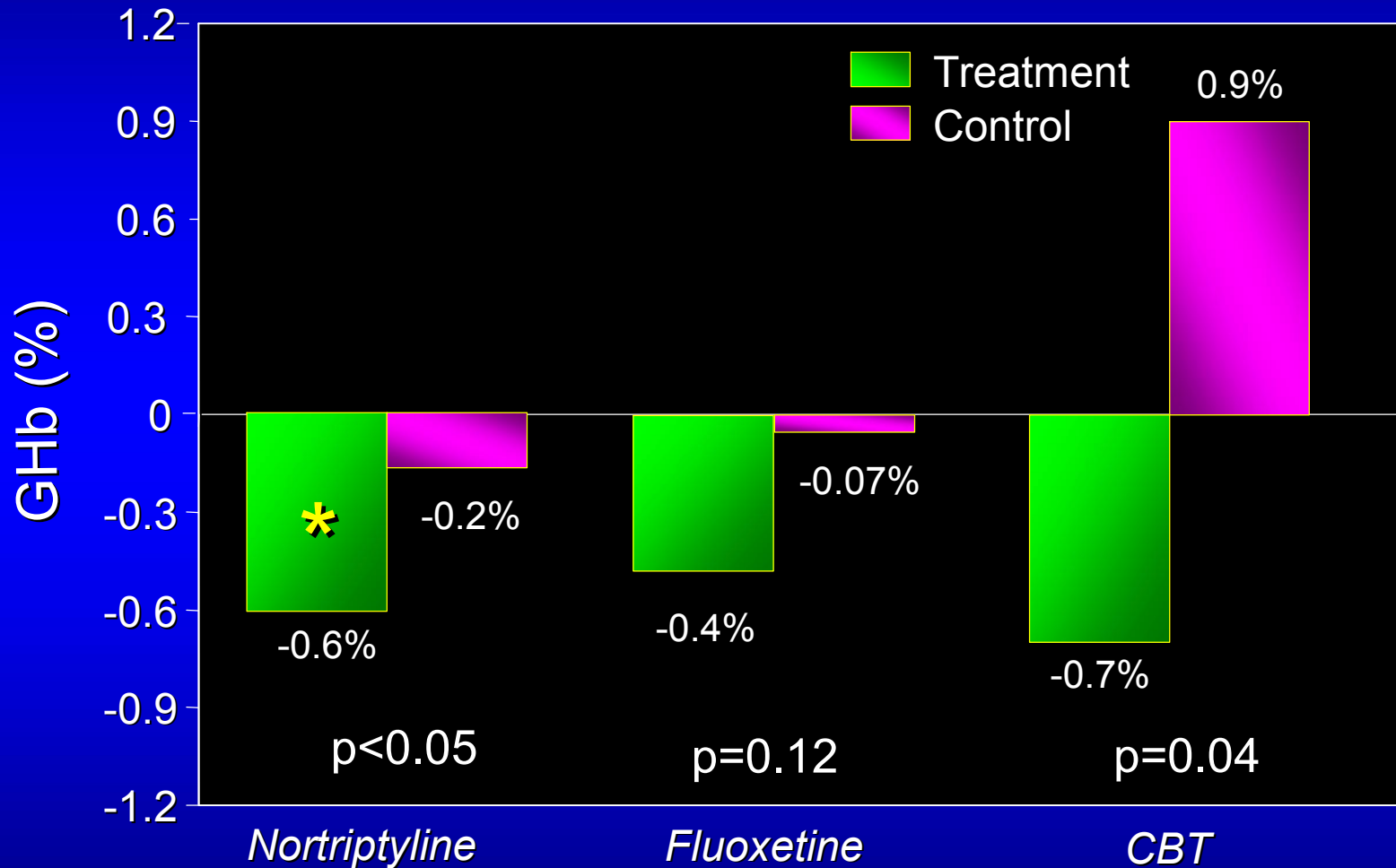
21.4

30.6

57.7

Treatment – Control (%)

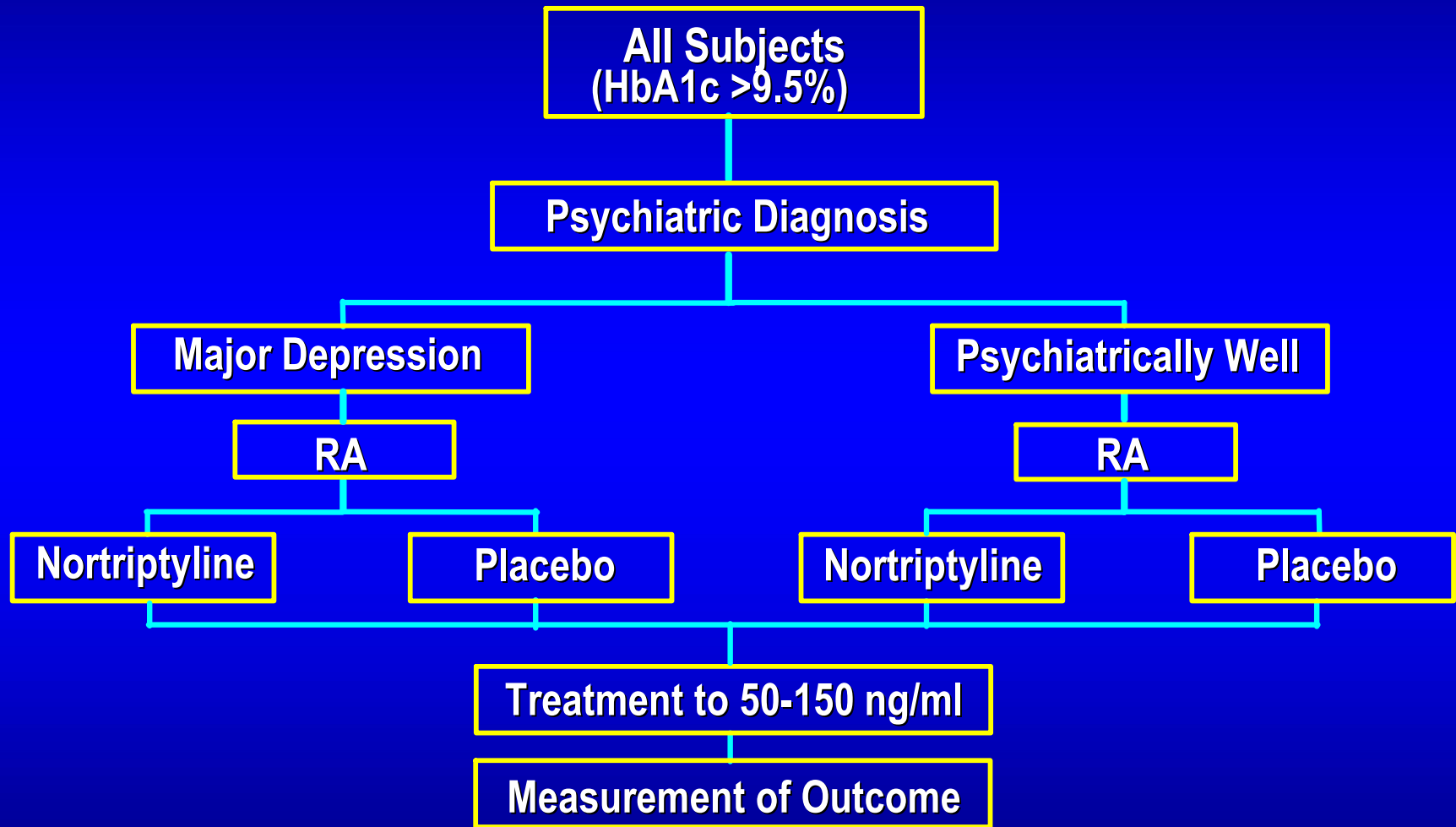
Treatment of Depression Produces Improvement in Glycemic Control



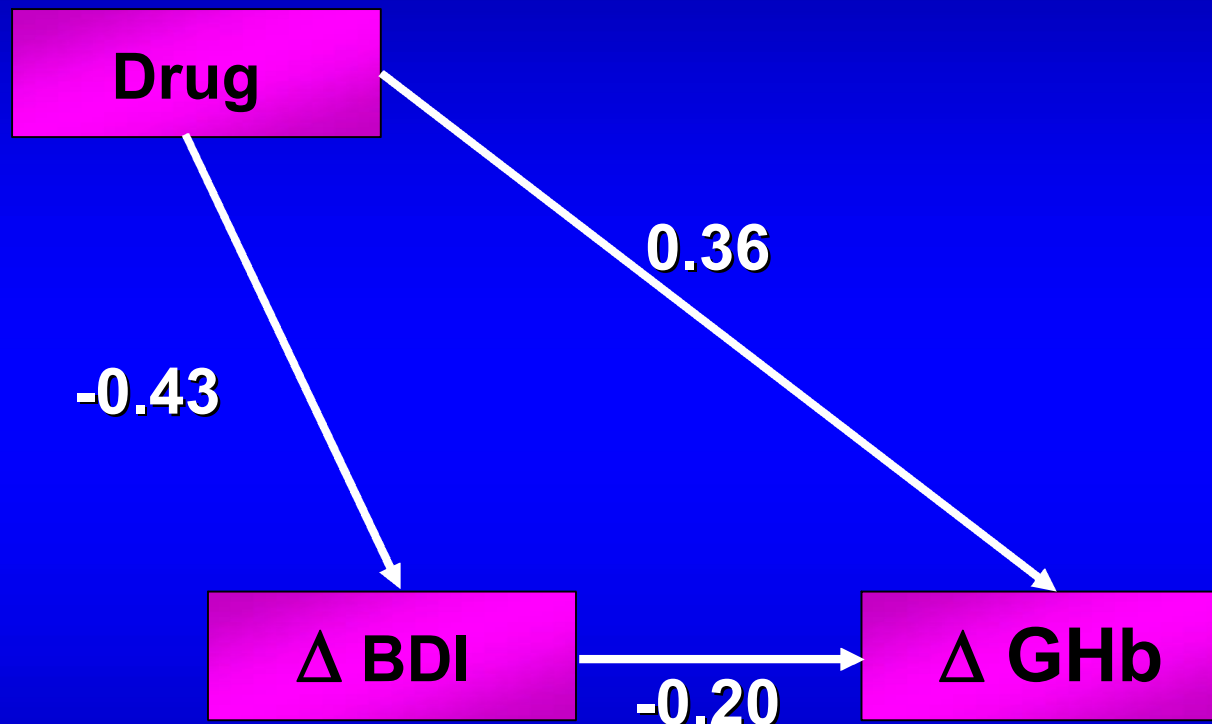
Treatment Trial

*Effect of depression improvement.

Nortriptyline in Diabetes

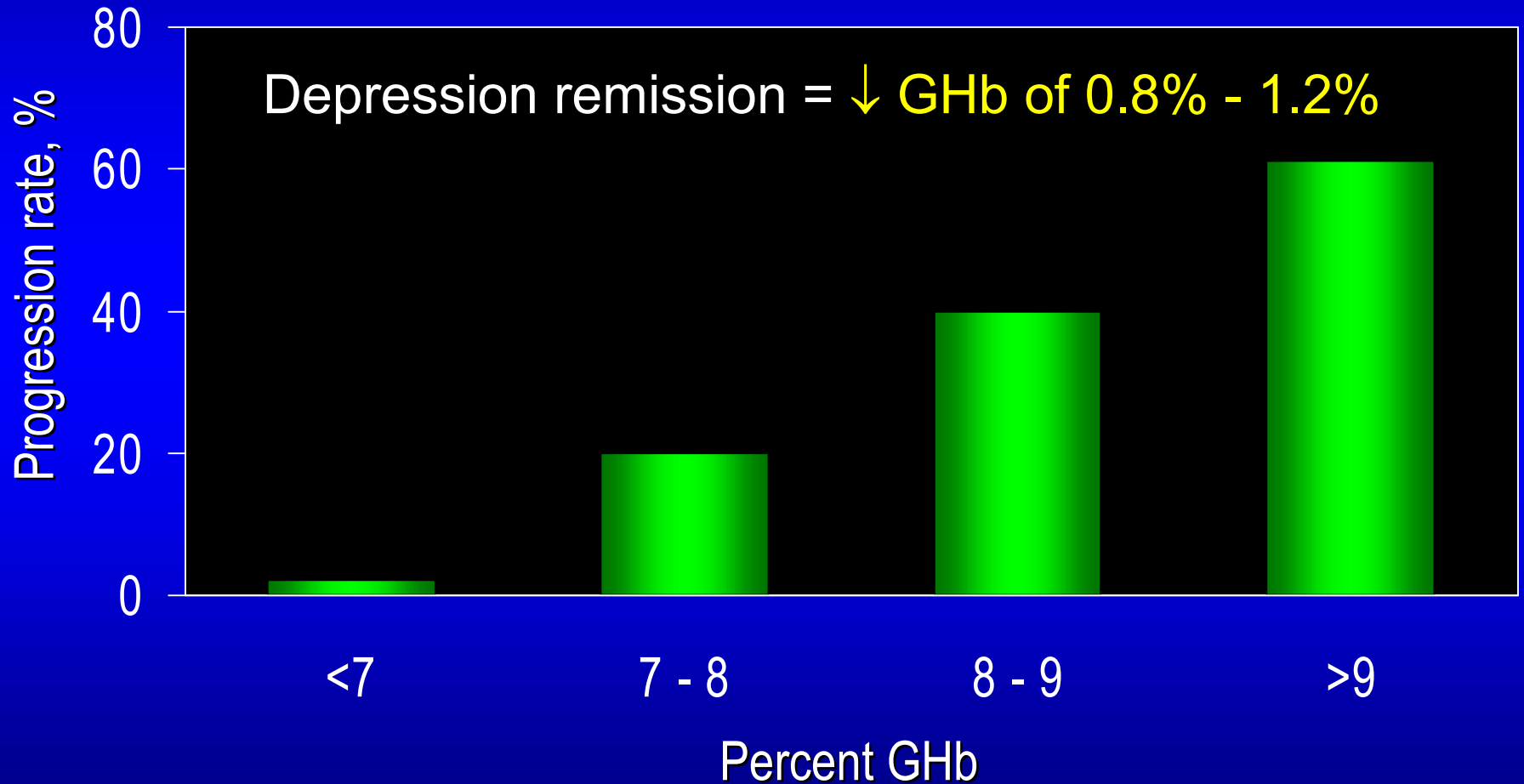


Effect of Depression Relief on GHb



Depression remission = \downarrow GHb of 0.8% - 1.2%

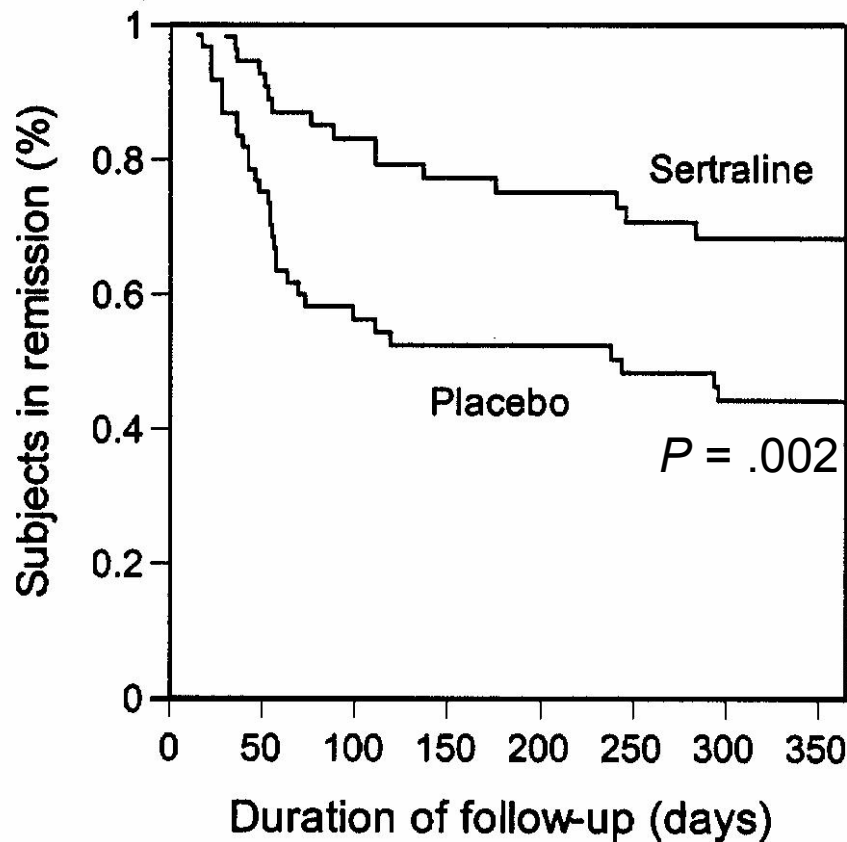
Progression Rate of Retinopathy as a Function of GHb



Depression in Diabetes is a Recurrent Problem

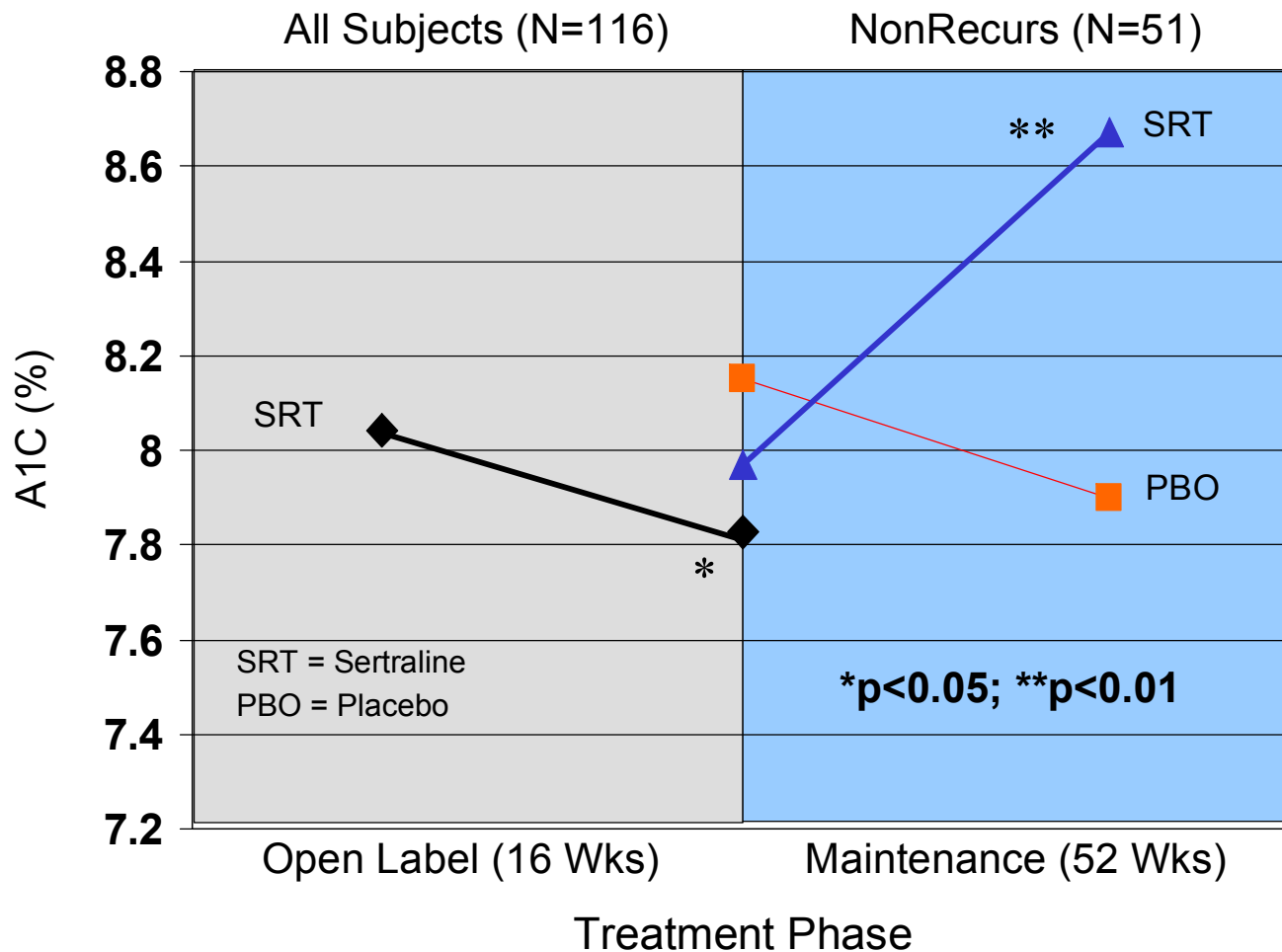
	Recurrence during 5 yr follow-up	Within 1 yr	# of depression episodes during follow-up
Lustman et al 1983	80	--	4.2
Lustman et al 1997	90	60	4.8
Psychiatric Samples	40-70	25-50	

Sertraline Maintenance Therapy for Prevention of Depression Recurrence

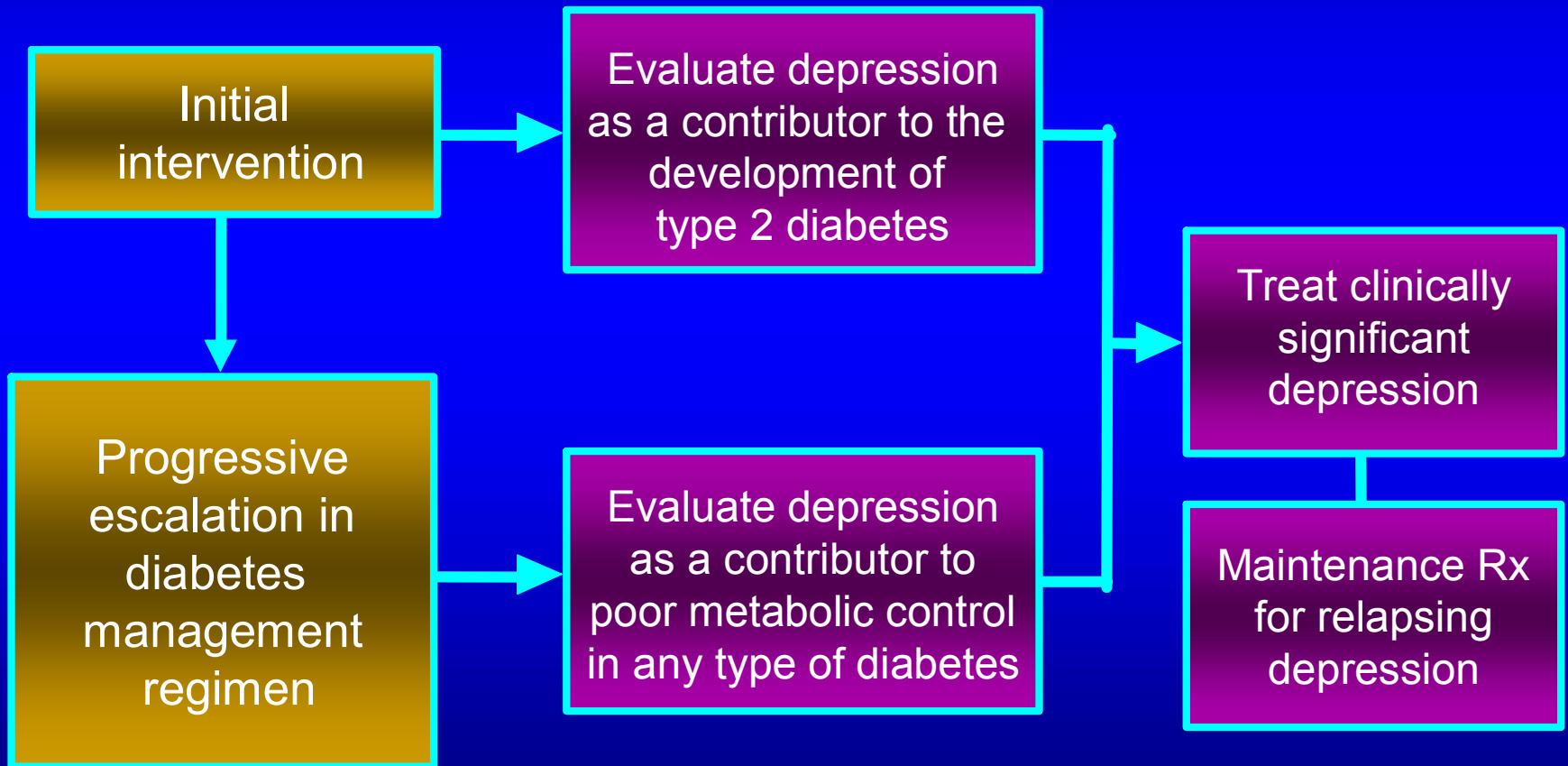


The proportion of patients remaining in remission was higher with sertraline than placebo (65% vs. 42%)

Change in A1C During Open Label and Maintenance Treatment



Optimizing Management of Diabetes and Depression



Summary

- Depression in diabetic patients is effectively treated using conventional approaches.
- The effects of depression treatment on mood and glycemic control are not always parallel nor stable over time.
- Response to therapy and reassessment for evidence of relapse or recurrence are essential; maintenance strategies are often required to achieve lasting remission.
- The interaction between depression and hyperglycemia may be bidirectional.