

# Addressing the Burden of Diabetes

2007  
Age-adjusted percent of adults ≥20 years old with diabetes

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## Standards of Medical Care 2011 and Beyond

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Chief Scientific and Medical Officer

# Diabetes Prevention and Treatment 2011 and Beyond

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- **Diabetes Burden**
  - Trends in prevalence, cost and health care burden
- **Diabetes Care 2011**
  - Diabetes standards of care – the ADA perspective
  - Glucose – Lipid – Blood Pressure control in diabetes
    - Implications of the ACCORD Trial
    - Treatment targets – Where do we stand?
- **Diabetes Prevention – The Path Forward**
- **Putting It All Together – Set for Success**

# The Burden of Diabetes

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## Impact on the Public Health and Health Care Costs

# The Burden of Diabetes

## Understanding the Diabetes Epidemic

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- **Worldwide burden of diabetes exceeds 190M individuals**
  - Affects ~8% of the US population (~24 million individuals)
  - Pre-diabetes in nearly 60 million (more than 90% unaware)
- **Public health impact**
  - 7<sup>th</sup> leading cause of death (2/3<sup>rd</sup> due to CVD)
  - Leading cause of amputation, dialysis, blindness
- **Health care impact**
  - Total costs of care **~\$174,000,000,000** (50% due to complications)
  - Accounts for 1/3<sup>rd</sup> of hospitalizations for CVD and 1/5<sup>th</sup> of clinical encounters

Numbers are estimated totals at all ages in the US. National Diabetes Fact Sheet, 2007.  
Available at: <http://www.cdc.gov/diabetes/pubs/factsheet07.htm>

# The Diabetes Epidemic

## Risk of Developing Diabetes for Children Born in 2000



- **Estimated lifetime risk of diabetes (if born in 2000)**
  - 1 in 3 children will develop diabetes
  - Higher risk in specific populations
    - 1 in 2 Hispanic, NA, African Am
- **Vital statistics**
  - Affects ~25% over age 60
  - Increasing most in age 40-59
  - Reduced life expectancy (at age 40) of 12 to 14 years

# Projecting the Future Diabetes Population Size and Related Costs for the U.S.

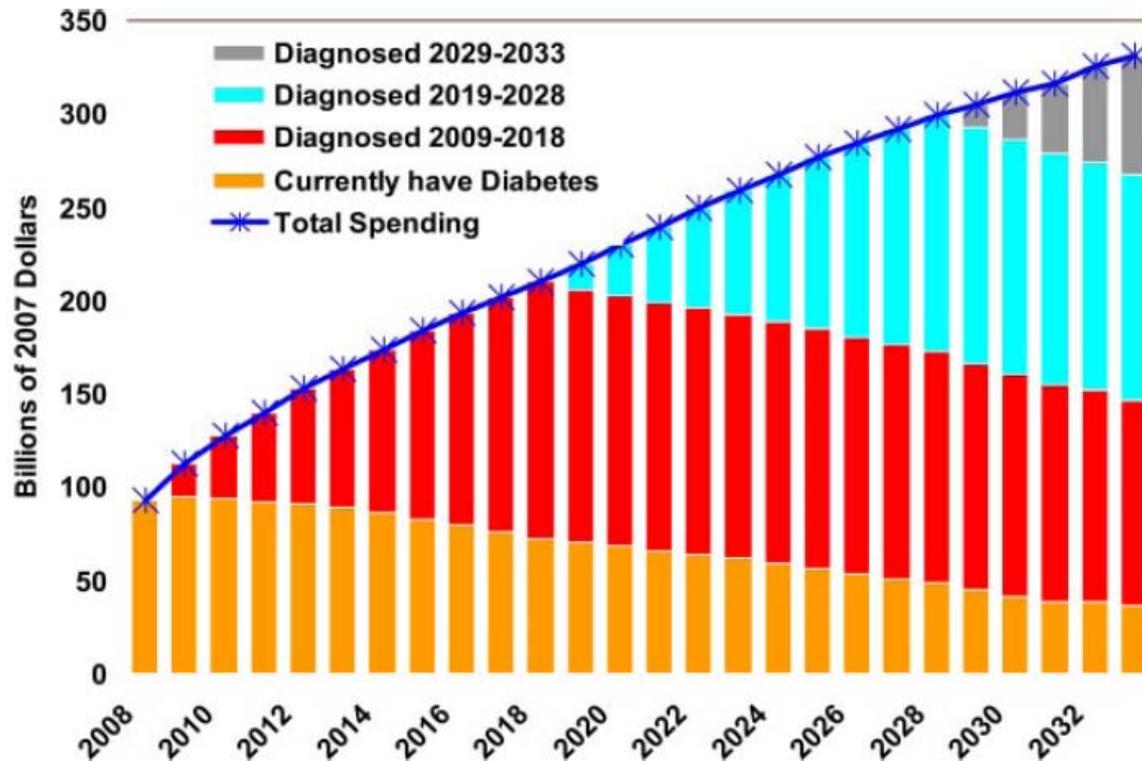
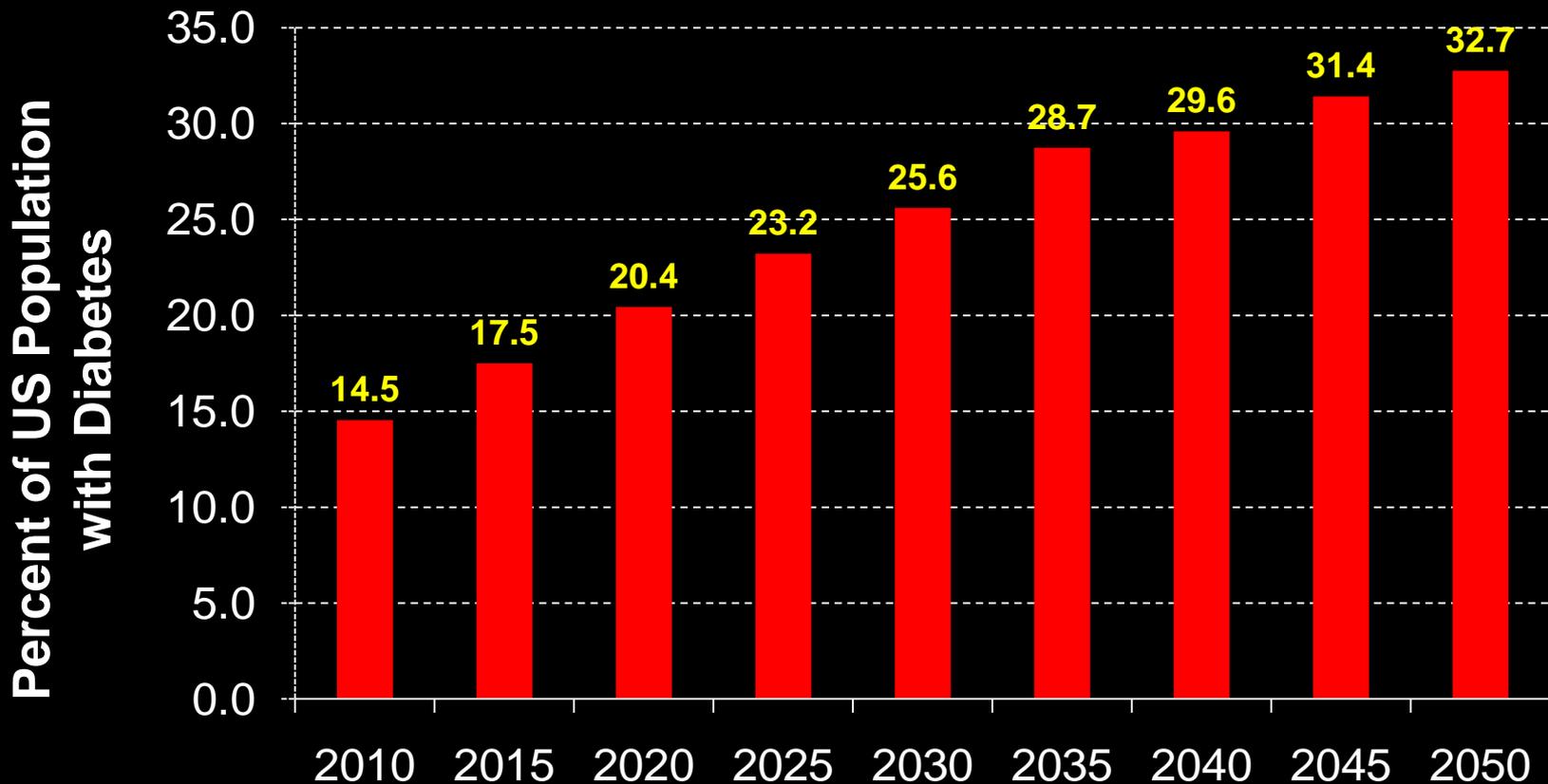


Figure 3—Projected direct spending on diabetes and its complications for different cohorts, 2008–2033. Reprinted with permission from Huang et al. (23).

Huang ES. *Diabetes Care* 32:2225–2229, 2009

# Projecting the Future Diabetes Population

## The Imperative for Change



Boyle JP. *Population Health Metrics* 2010, 8:29doi:10.1186/1478-7954-8-29  
Published: 22 October 2010

# Diabetes Care 2011

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## Screening and Detection

### The Standards of Medical Care in Diabetes

### Glucose – Lipids – Blood Pressure

# Executive Summary: Standards of Medical Care in Diabetes—2011

- **Diagnosis of diabetes includes addition of A1C testing**
  - A1C  $\geq$  6.5% diagnostic of diabetes, added to FPG and OGTT
  - “Categories at High Risk” = FPG 100-125, A1C of 5.7–6.4%
- **Diabetes self-management**
  - Prevention and delay, glucose monitoring and A1C
  - DSME and Nutrition
- **Complications management – Risk Factors**
  - **Treatment targets** – screening, detection, treatment of complications
- **Others**
  - Psychosocial care, bariatrics, hypoglycemia, age specific, hospital care

American Diabetes Association. *Diabetes Care* 34 (Suppl 1), 2011

# Standards of Diabetes Care:

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## Implications of Recent Outcome Trials

### A1C – Blood Pressure – Lipids

# Treatment Targets for Adults with Diabetes

## Minimizing Micro and Macrovascular Disease Risk

### Measures

### Targets

- **A1C**

**< 7%**

- Pre-meal glucose

90 – 130 mg/dl

- Peak post-meal glucose

< 180 mg/dl

- **Blood Pressure**

**< 130/80 mm Hg**

- **LDL-c**

**< 100 mg/dl**

- Triglycerides

< 150 mg/dl

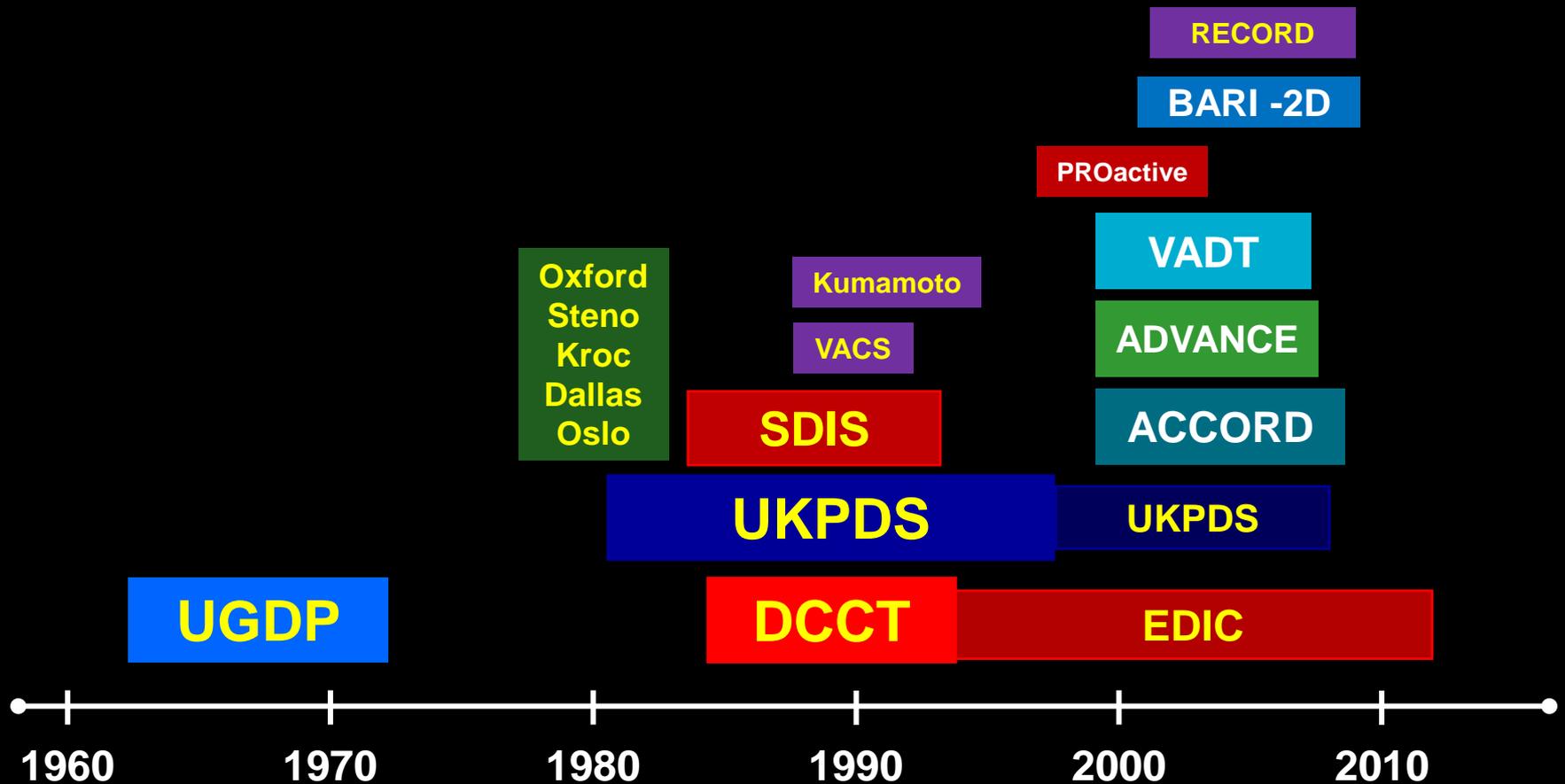
- HDL-c

> 40 mg/dl

American Diabetes Association. *Diabetes Care* 34 (Suppl 1), 2011

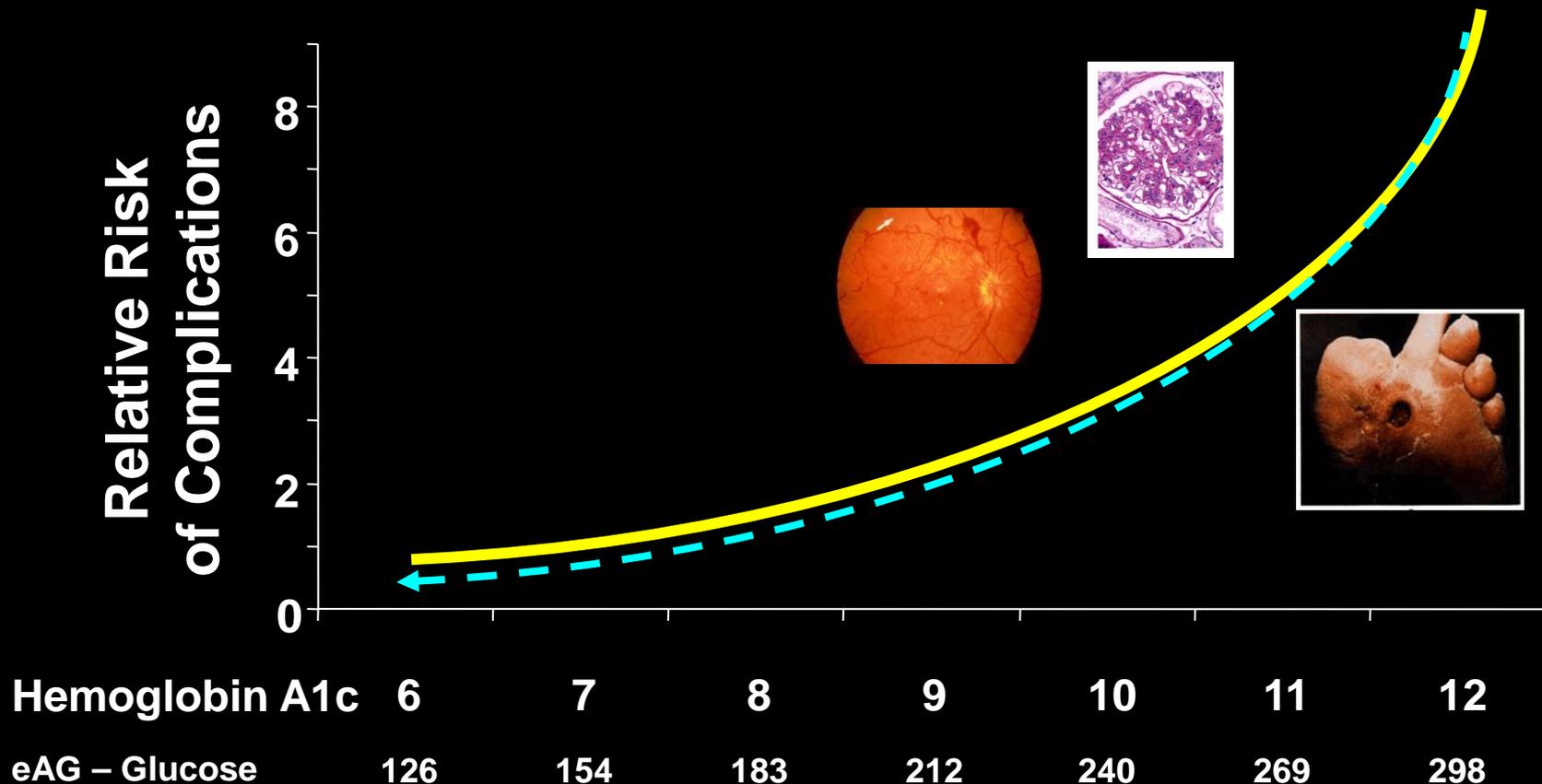
# Glycemic Control in Diabetes

## A Brief History of Intervention Trials



# Complications Risk in Diabetes

## The Impact of Intensive Glycemic Control

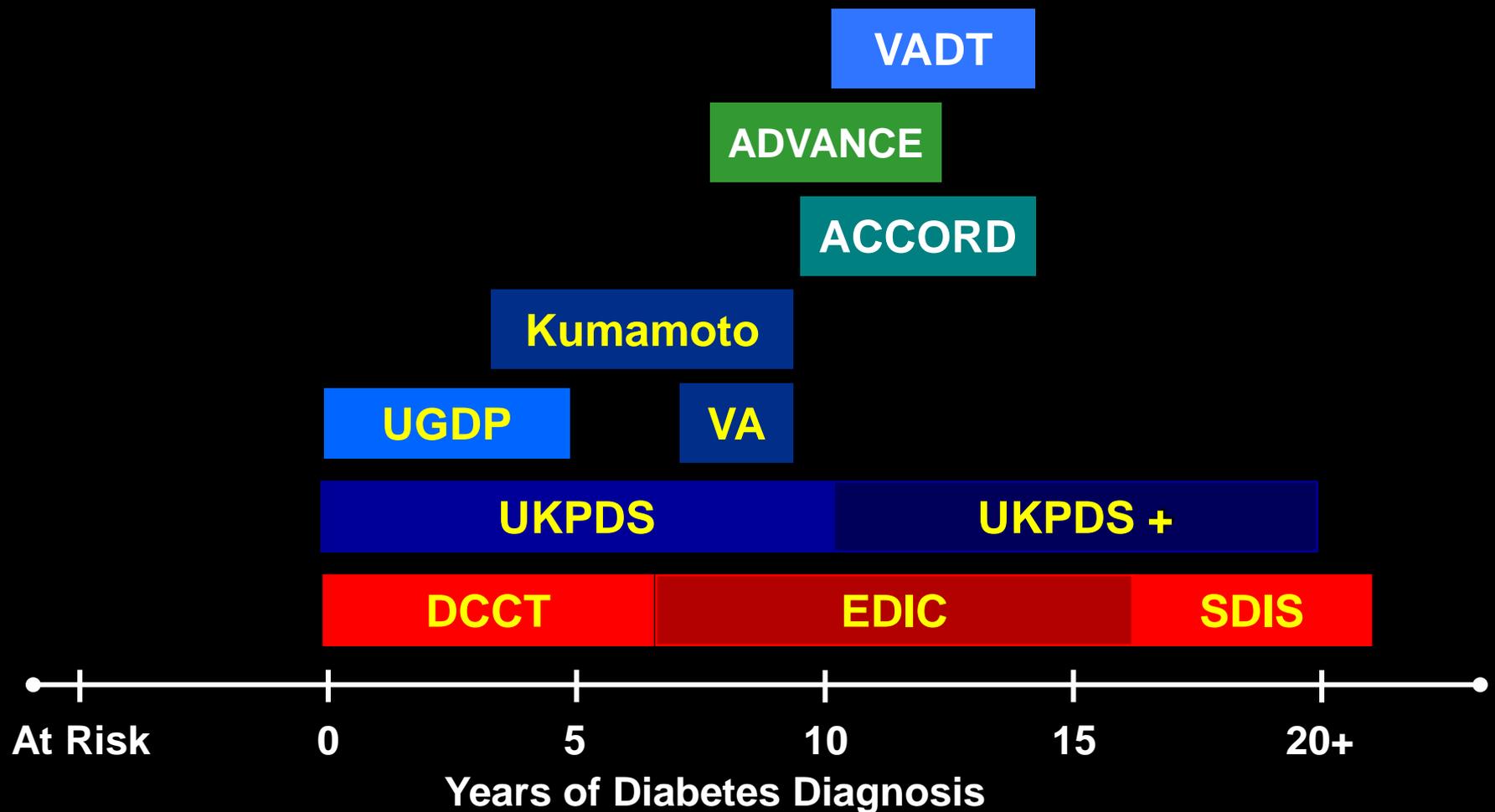


DM Kendall. International Diabetes Center

Adapted from: Skyler JS. *Endocrinol Metab Clin North Am.* 1996 Jun;25(2):243-54.

DCCT Study Group. *N Engl J Med* 329:977, 1993. UKPDS 35. Stratton IM. *BMJ* 321:405-412, 2000.

# Glycemic Control for Microvascular Complications: Is Late Too Late?



# Early Intensive Diabetes Therapy: Reduction in Microvascular Complications

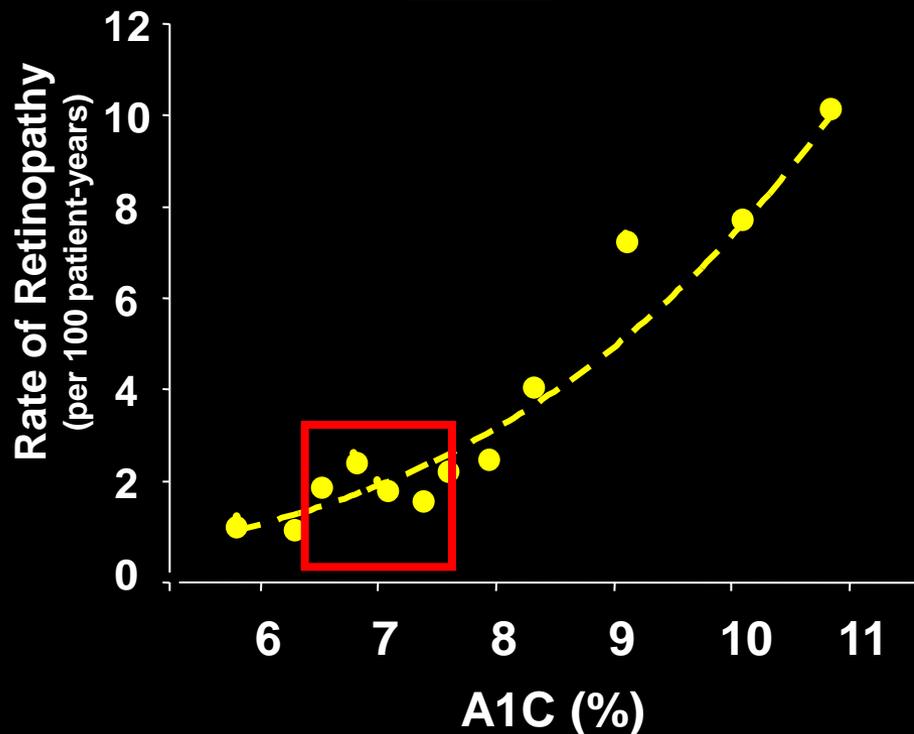
	<u>DCCT</u>	<u>Kumamoto</u>	<u>UKPDS</u>
<b>HbA1c</b>	<b>9 → 7.1%</b>	<b>9+ → 7.2%</b>	<b>7.9 → 7%</b>
Retinopathy	63%	69%	17-29%
Nephropathy	<b>54%</b>	<b>70%</b>	<b>24-33%</b>
Neuropathy	60%	Improved	-
CV disease	NS	-	16% (NS)

DCCT Research Group. *N Engl J Med.* 1993;329:977-986.  
 Ohkubo Y, et al. *Diabetes Res Clin Pract.* 1995;28:103-117.  
 UKPDS 33: *Lancet* 1998; 352, 837-853.

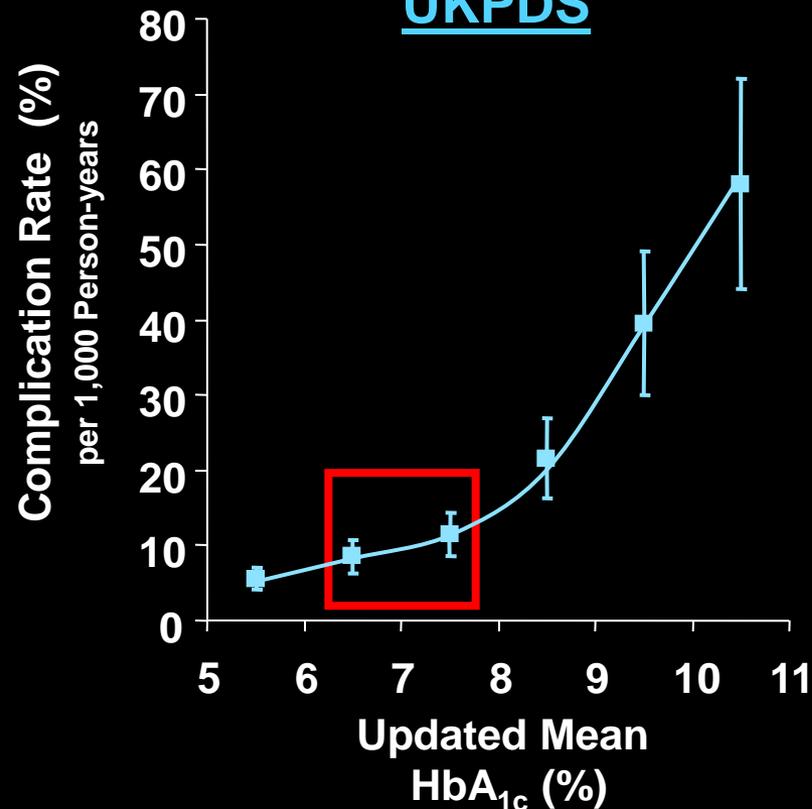
# DCCT and UKPDS

## Glycemic Control and Microvascular Risk

### DCCT



### UKPDS



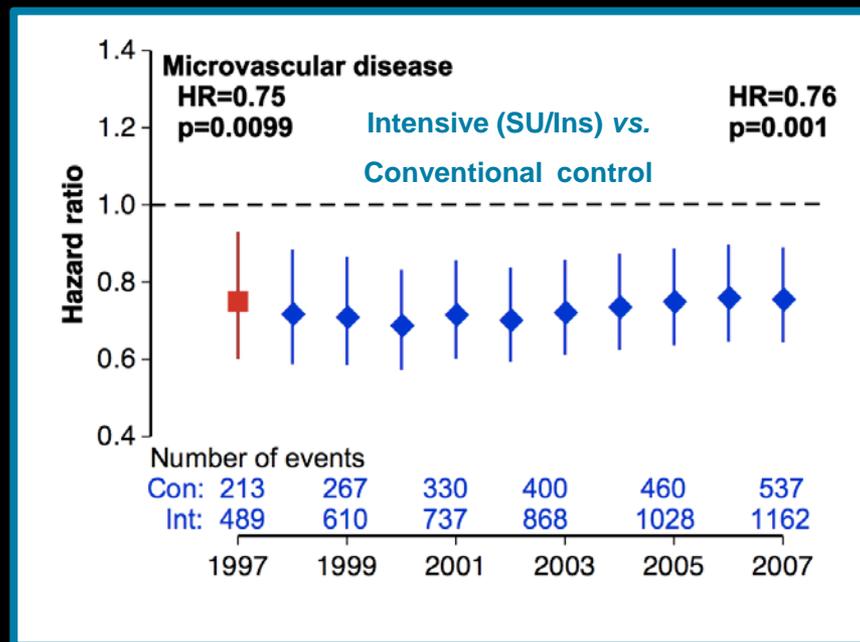
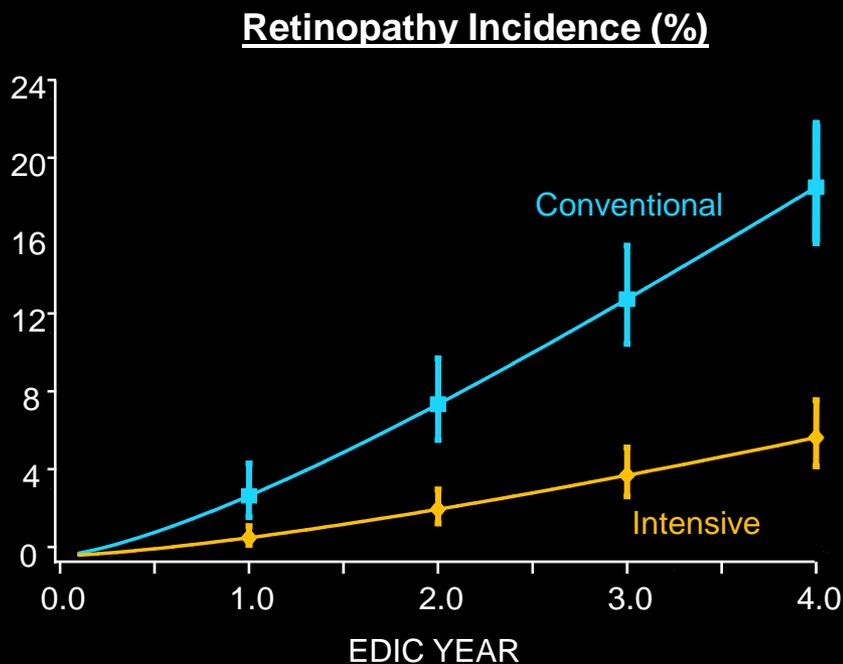
DCCT Study Group. *N Engl J Med* 329:977, 1993  
UKPDS 35. Stratton IM. *BMJ*. 2000;321:405-412.

# The Durable Effect of Early Intervention

## Long Term Follow up from EDIC and UKPDS

Follow up cohort with similar glycemic control for 4-10+ years

A1C achieved = ~8.0%



EDIC Research Group. *N Engl J Med* 2000;342:381-9  
 Holman RR. *N Engl J Med*. 2008;359:1577-89

The NEW ENGLAND JOURNAL of MEDICINE

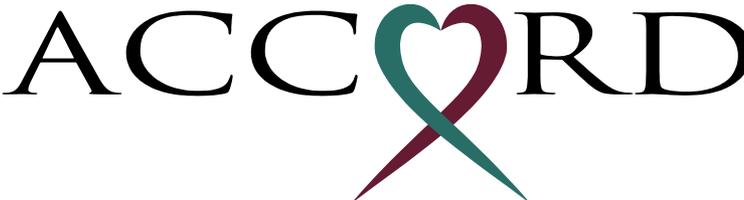
ORIGINAL ARTICLE

# Effects of Medical Therapies on Retinopathy Progression in Type 2 Diabetes

The ACCORD Study Group and ACCORD Eye Study Group\*

*Action to Control Cardiovascular Risk in Diabetes*

ACCORD



ACCORD Study Group. Chew EY. N Engl J Med. 2010 Jul 15;363(3):233-44. Epub 2010 Jun 29.

# Proportion of Participants with Diabetic Retinopathy Progression at 4 years

	Blood Pressure		Lipid		N=2856 Total
Glycemia	Intensive	Standard	Fenofibrate & Simvastatin	Placebo	TOTALS
Intensive	<b>9.2%</b> (29/315)	<b>8.1%</b> (25/308)	<b>5.3%</b> (21/400)	<b>7.1%</b> (29/406)	<b>7.5%</b> (104/1429)
Standard	<b>11.4%</b> (38/332)	<b>9.4%</b> (29/308)	<b>7.6%</b> (31/406)	<b>13.4%</b> (51/381)	<b>10.4%</b> (149/1427)
<b>TOTALS</b>	<b>10.4%</b> (67/647)	<b>8.8%</b> (54/616)	<b>6.5%</b> (52/806)	<b>10.2%</b> (80/787)	8.9% (253/2856)

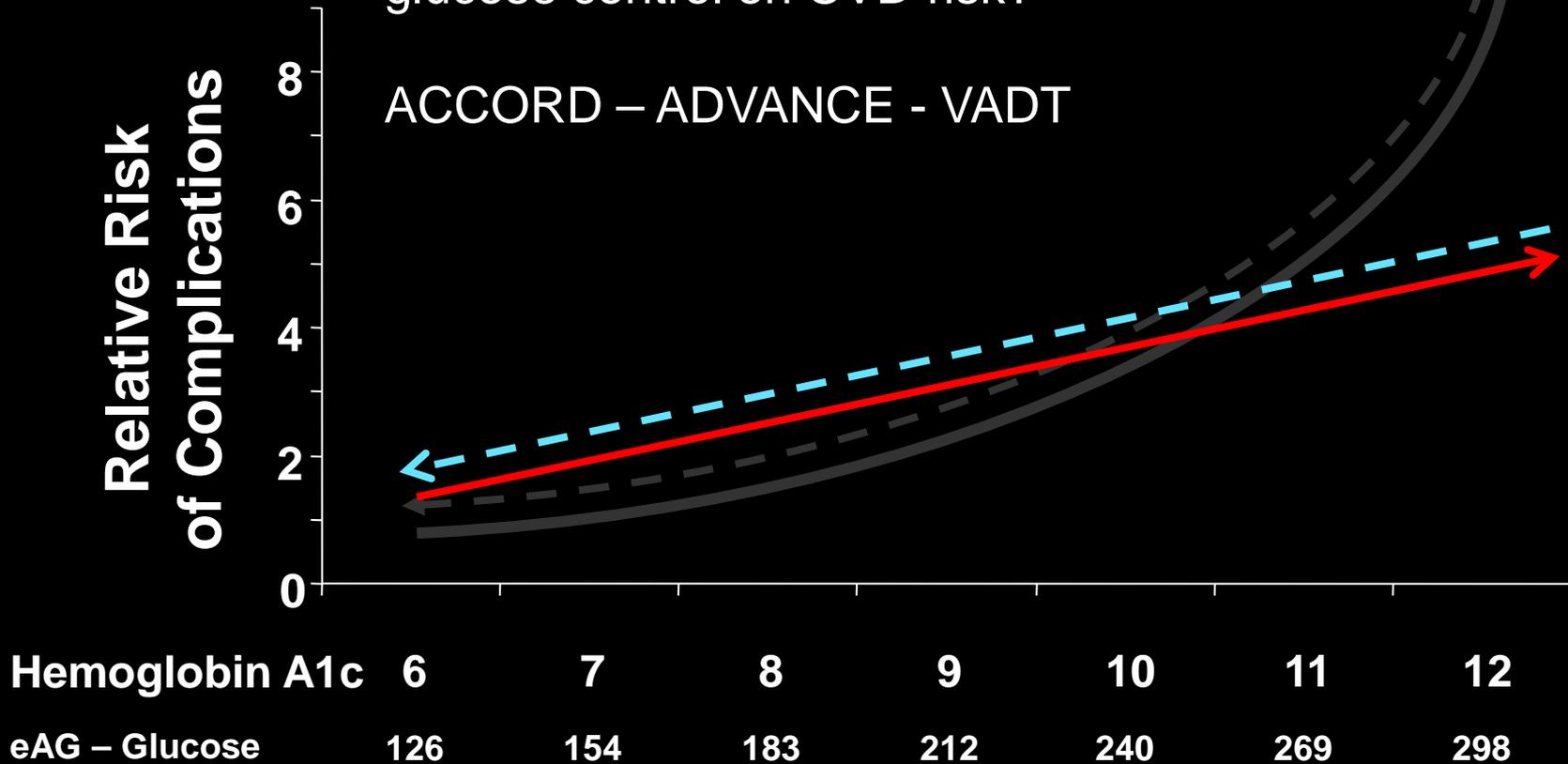
ACCORD Study Group. Chew EY. N Engl J Med. 2010 Jul 15;363(3):233-44. Epub 2010 Jun 29.

# Complications Risk in Diabetes

## The Impact of Intensive Glycemic Control

What is the impact of intensive glucose control on CVD risk?

ACCORD – ADVANCE - VADT



DM Kendall. International Diabetes Center

Adapted from: Skyler JS. *Endocrinol Metab Clin North Am.* 1996 Jun;25(2):243-54.

DCCT Study Group. *N Engl J Med* 329:977, 1993. UKPDS 35. Stratton IM. *BMJ* 321:405-412, 2000.

# A Broader View of Complications and Diabetes

## Implications of ACCORD, ADVANCE and VADT

Study	A1C	Microvascular		CVD	Mortality	
UKPDS	9 → 7.9 → 7	↓	↓	↔	↓	↔
DCCT/EDIC	9 → 7.1	↓	↓	↔	↓	↔
ACCORD	7.5 → 6.4	↓		↔	↑ ?	
ADVANCE	7.3 → 6.5	↓		↔	↔	
VADT	8.4 → 6.9	↓		↔	↔	

Adapted from Bergenstal RM, Bailey C and Kendall DM. *Am J Med* 123:374e9-e18, 2010

UK Prospective Diabetes Study (UKPDS) Group. *Lancet*. 1998;352:854-865.

Holman RR. *N Engl J Med*. 2008 Oct 9;359(15):1577-89. DCCT Research Group. *N Engl J Med* 329:977-986, 1993

Nathan DM, et al. *N Engl J Med*. 2005;353:2643-2653. Gerstein HC, et al. *N Engl J Med*. 2008;358:2545-2559.

Patel A, et al. *N Engl J Med*. 2008;358:2560-2572. Duckworth W et al *N Engl J Med* 2009;360:129-39

EY Chew for ACCORD. *N Engl J Med* (10.1056/NEJMoa1001288) was published on June 29, 2010, at NEJM.org.



Initial Trial



Long Term Follow-up

# Identifying Higher Risk Patients

## Intensive Glycemic Control in Type 2 Diabetes

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- **Conventional Wisdom:**

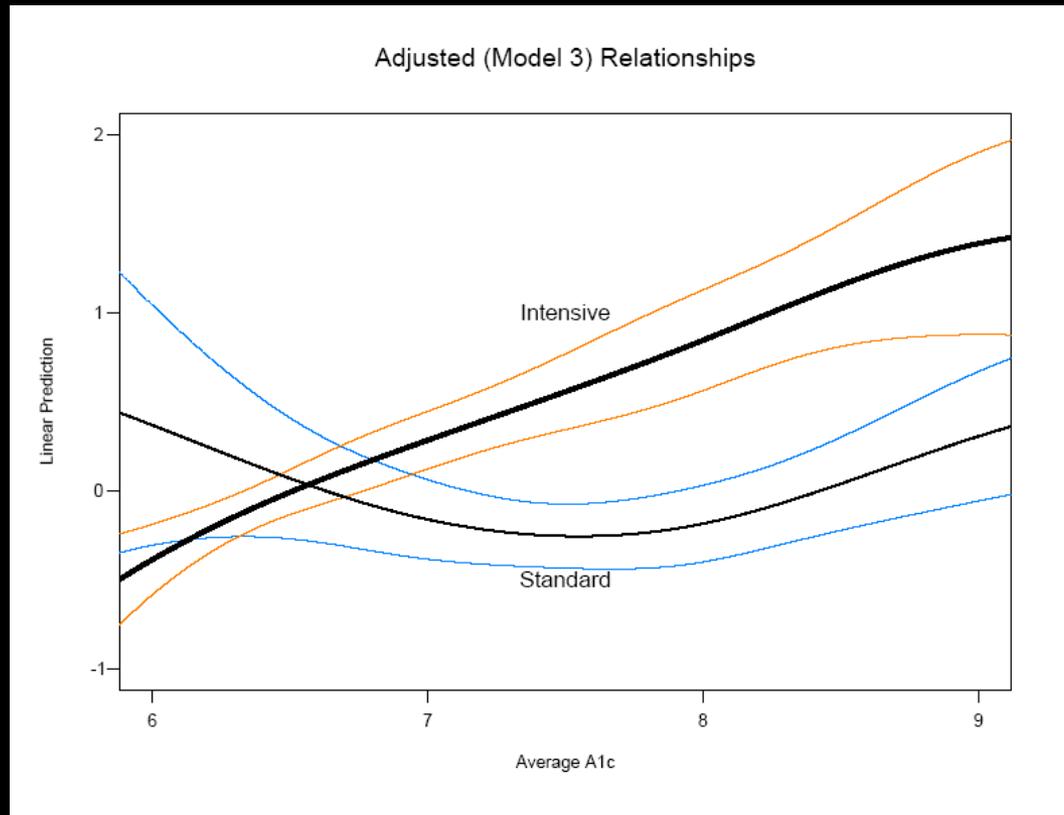
- Older individuals with established CVD NO
- Those who achieved lower A1C values NO
- Use of insulin therapy NO
- Individuals with longer duration diabetes MAYBE

- **Who May Be at Risk with more intensive Rx**

- Longstanding poor control YES
- History of severe hypoglycemia YES
- Those less responsive to intensive Rx MAYBE

# Epidemiologic Relationships Between A1c and All-cause Mortality in the ACCORD Trial

- Does A1C achieved predict a risk for all-cause mortality?



Riddle M et al. Diabetes Care. 2010 May;33(5):983-90

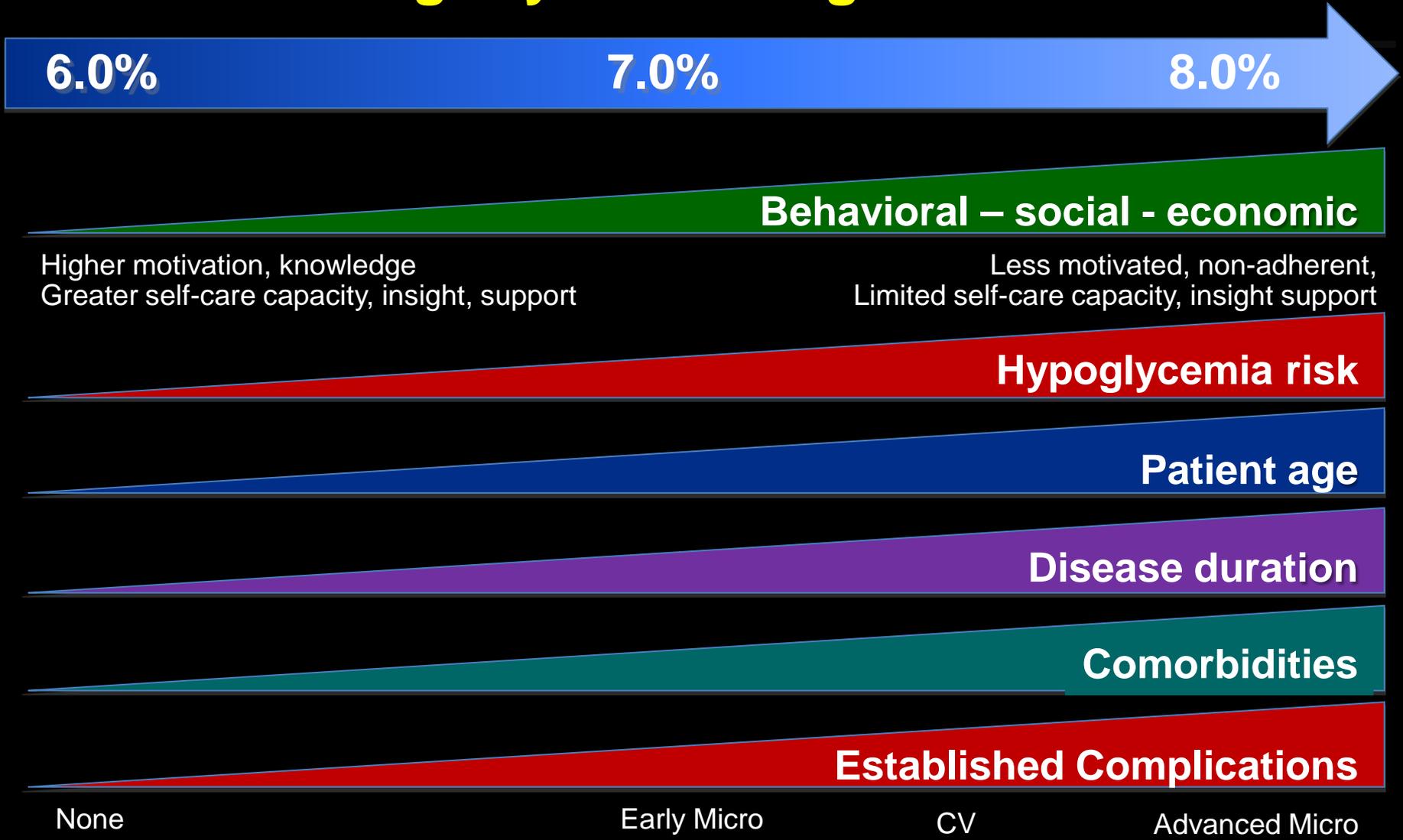
# Glycemic Targets in Adults

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- Lowering of A1C to at or below 7%
  - Shown to reduce microvascular complications of diabetes
  - *Does not* reduce the risk of CVD events in short term studies
  - *Does not* significantly increase mortality
  - If initiated soon after diagnosis, possible long-term reduction in CVD
- Analysis suggest a small (but incremental) benefit in microvascular outcomes with A1C values closer to normal
  - Later application of intensive treatment may reduce the magnitude of impact
- Individualization of treatment critical
  - Both lower and higher glycemic targets may be appropriate

Skyler JS. *Diabetes Care*. 2009;32(1):187-92 ADA. *Diabetes Care*. *Diabetes Care* 2011;34(suppl 1):S19.

# Individualizing Glycemic Targets in Diabetes



Adapted from Ismael-Beigi F. Ann Intern Med. 2011;154(8):554-9.

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“Everything should be made as  
simple as possible,  
but no simpler”

A. Einstein

# Diabetes and Glycemic Control

## A Rational Approach to A1C Targets

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As low as possible

As early as possible

For as long as possible

As safely as possible

And as rationally as possible

*And in the setting of multi-risk factor management*

# **Blood Pressure Control and Lipid Management in Diabetes**

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**Treatment Targets – Treatment Approaches  
Implications of ACCORD and ADVANCE**

# Treatment Targets for Adults with Diabetes

## Minimizing Micro and Macrovascular Disease Risk

### Measures

- **A1C**
  - Pre-meal glucose
  - Peak post-meal glucose

### Targets

**< 7%**

90 – 130 mg/dl

< 180 mg/dl

- **Blood Pressure**

**< 130/80 mm Hg**

- **LDL-c**

**< 100 mg/dl**

- Triglycerides

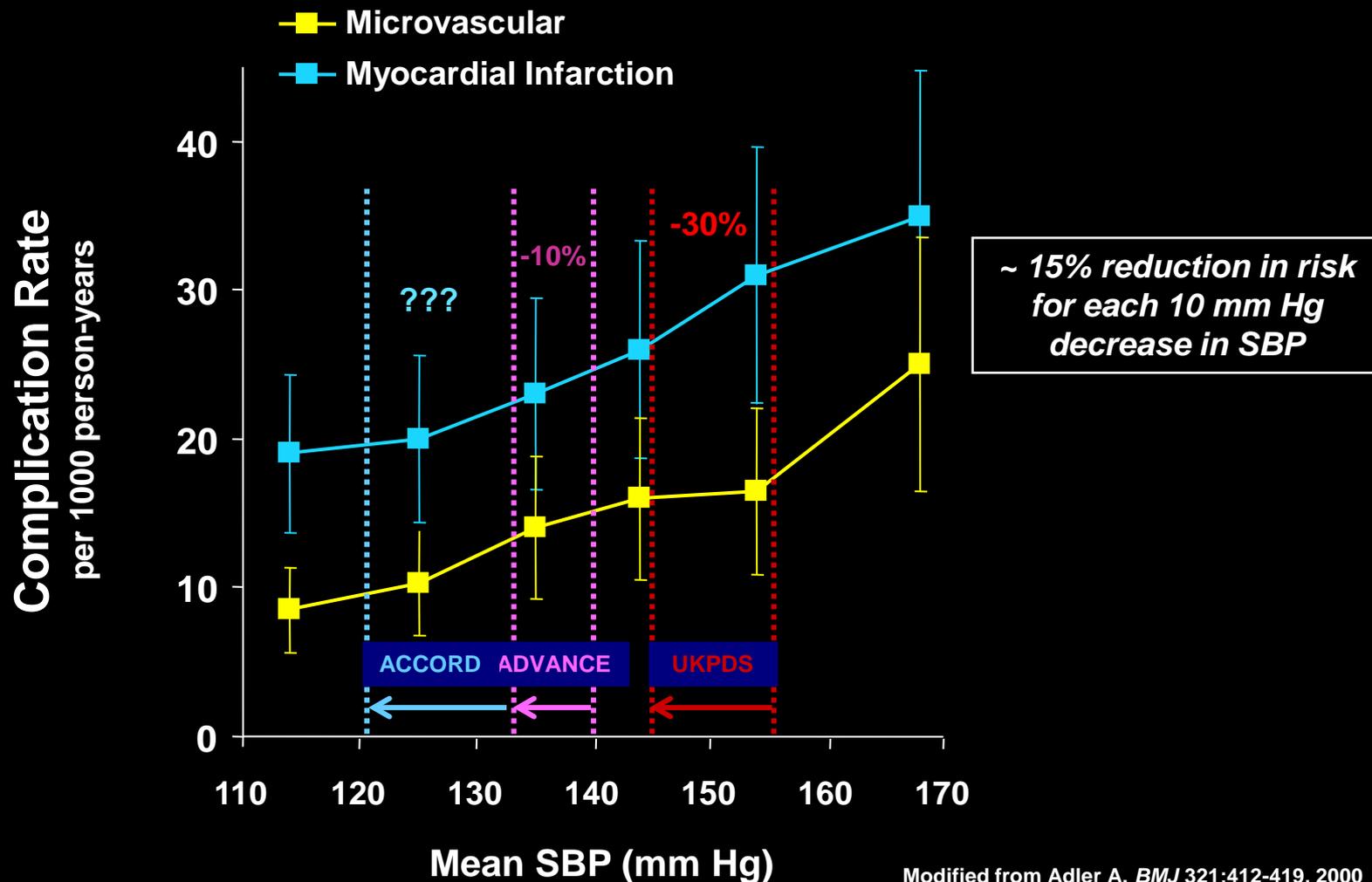
< 150 mg/dl

- HDL-c

> 40 mg/dl

American Diabetes Association. *Diabetes Care* 34 (Suppl 1), 2011

# Type 2 Diabetes and Blood Pressure: BP Control and Risk in the ACCORD and ADVANCE Era



Modified from Adler A. *BMJ* 321;412-419, 2000

# Multi-Risk Factor Intervention in Diabetes

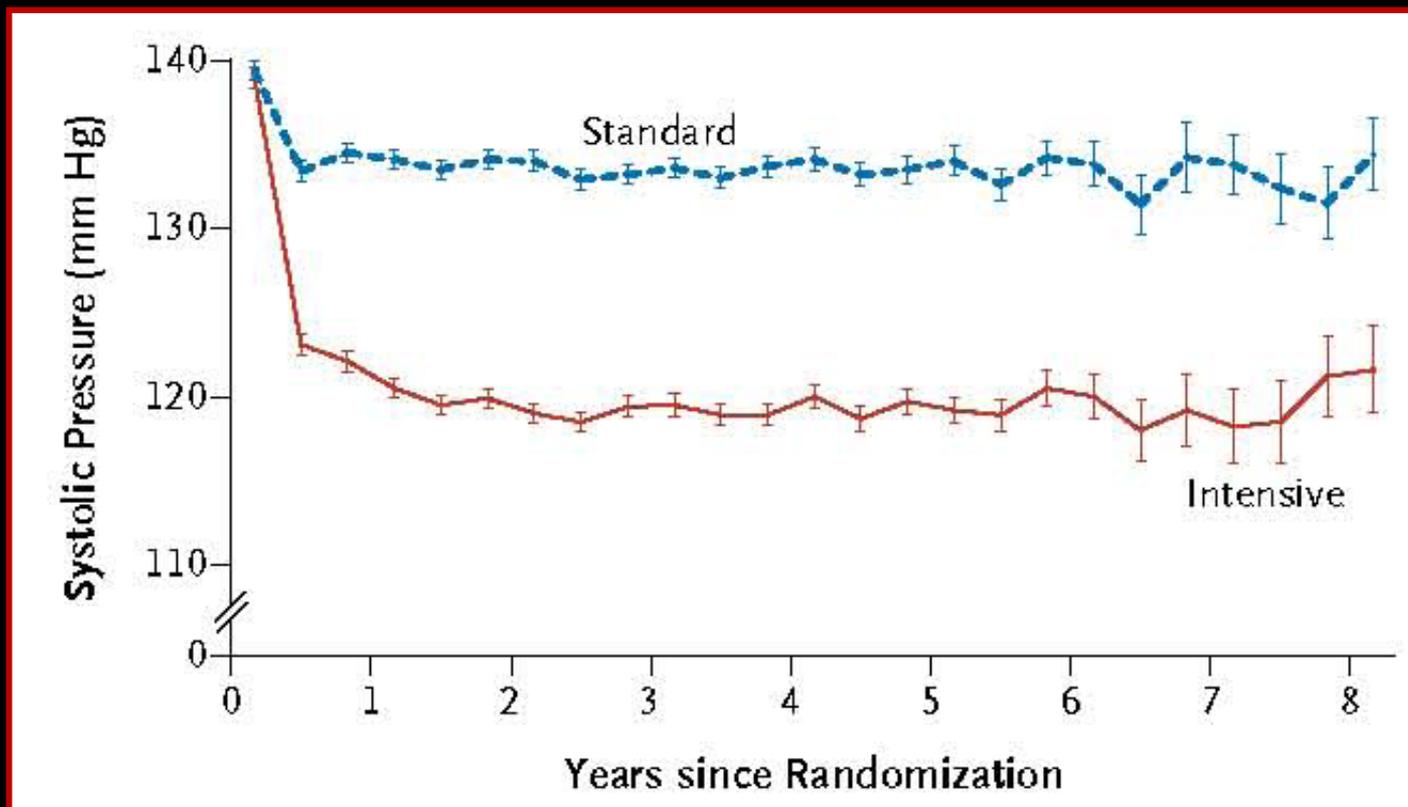
## The ACCORD Trial - Blood Pressure

	BP Trial		Lipid Trial		
	Intensive (SBP<120)	Standard (SBP<140)	Group A Statin only	Group B Statin+Fibrate	
Intensive Glycemic Control (HbA1c<6%)	1178	1193	1383	1374	<b>5128*</b>
Standard Glycemic Control (HbA1c 7-7.9%)	1184	1178	1370	1391	
	<b>2362*</b>	<b>2371*</b>	<b>2753*</b>	<b>2765*</b>	<b>10,251</b>

\*Primary analysis compares marginals for main effects

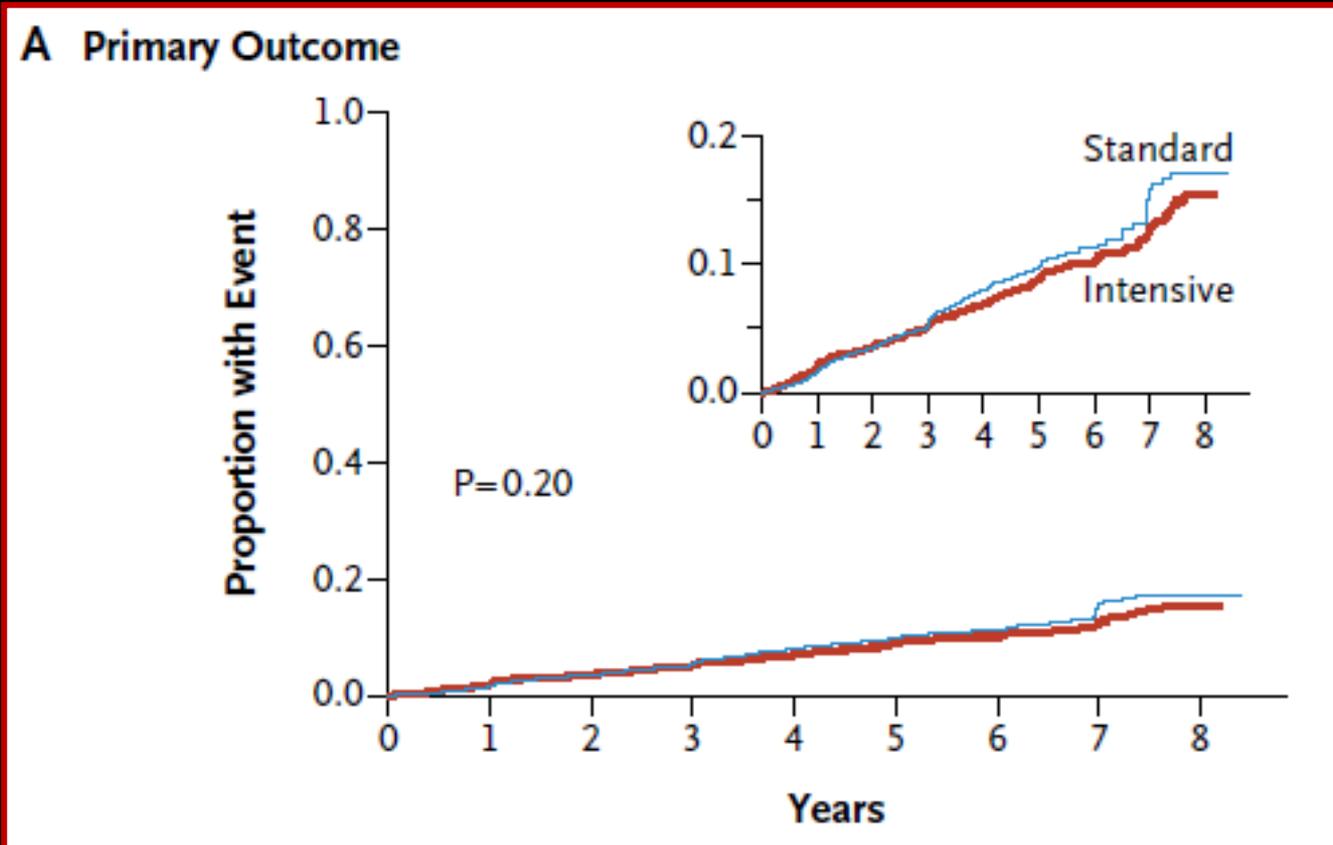
ACCORD Study Group. *Am J Cardiol* 99(12A):21i-33i, 2007.

# Effects of Intensive Blood Pressure Control The ACCORD Trial



ACCORD Study Group. *N Engl J Med* 2010. Published on March 14, 2010, at NEJM.org.

# Effects of Intensive Blood Pressure Control The ACCORD Trial



ACCORD Study Group. *N Engl J Med* 2010. Published on March 14, 2010, at NEJM.org.

# Multi-Risk Factor Intervention in Diabetes

## The ACCORD Trial - Lipids

	BP Trial		Lipid Trial		
	Intensive (SBP<120)	Standard (SBP<140)	Group A Statin only	Group B Statin+Fibrate	
Intensive Glycemic Control (HbA1c<6%)	<p><b>No significant added benefit (in reducing MI, stroke or CVD death) with addition of fibrate to statin therapy</b></p> <p>The ACCORD Study Group. <i>N Engl J Med</i> 2010. Published at <a href="http://www.nejm.org">www.nejm.org</a> March 14, 2010 (10.1056/NEJMoa1001286)</p>				5128*
Standard Glycemic Control (HbA1c 7-7.9%)					5123*
	2362*	2371*	2753*	2765*	10,251

\*Primary analysis compares marginals for main effects

ACCORD Study Group. *Am J Cardiol* 99(12A):21i-33i, 2007.

# ACCORD Blood Pressure and Lipid Studies Summary and Conclusions

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- Targeting SBP <120 mm Hg as compared to <140 mm Hg
  - Does not support broad use more intensive control of SBP to limit rates of major CVD events
  - More intensive BP control may reduce stroke and progression of CKD
  - Suggests that general targets below current standard are unnecessary
- Combination fibrate+ statin therapy (as compared to statin alone)
  - No evidence of a reduction in major CVD events
  - Subgroup analyses identify *potential benefit* in those with lower HDL-c (< 34 mg/dl) and higher TG (> 204 mg/dl)

# ADA – Summary of Recommendations for Adults with Diabetes

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## Measures

## Targets

- **A1C**
  - Pre-meal glucose **< 7%**
  - Peak post-meal glucose **90 – 130 mg/dl**
  - **< 180 mg/dl**
- **Blood Pressure:** **< 130/80 mm Hg**
- **LDL-c** **< 100 mg/dl**
  - Triglycerides **< 150 mg/dl**
  - HDL-c **> 40 mg/dl**

American Diabetes Association. *Diabetes Care* 34 (Suppl 1), 2011

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“So after observation and analysis, when you find that anything agrees with reason and is conducive to the good and benefit of one and all, then accept it and live up to it.”

Buddha

# Screening, Detection and Prevention of Type 2 Diabetes

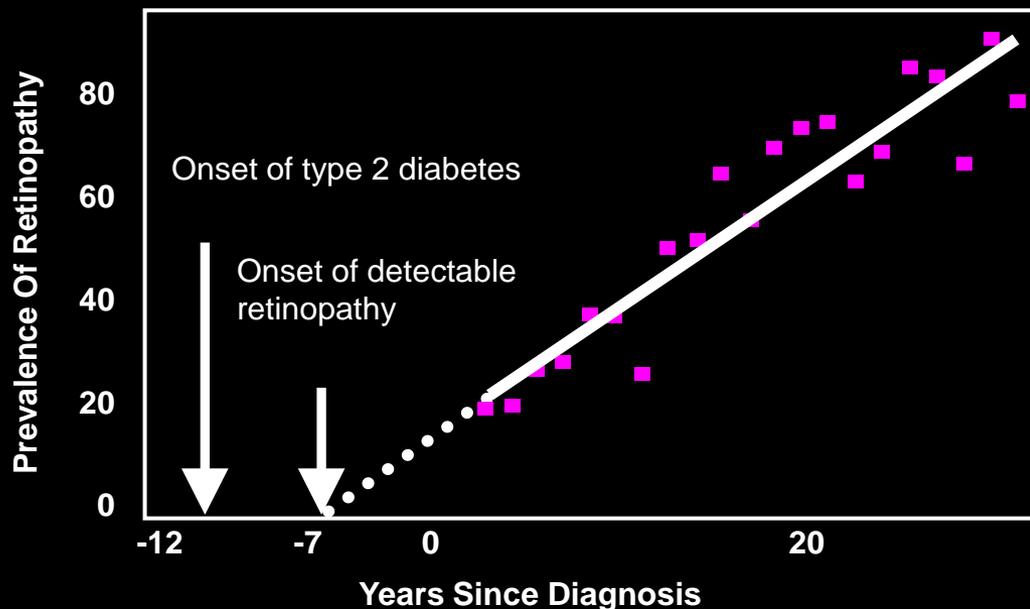
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## The Path Forward

# Diabetes Prevention

## Screening For Diabetes and Pre-Diabetes

- Why Screen for Diabetes and Pre-Diabetes?
  - Common clinical condition – roughly 1 in 4 undiagnosed
    - Simple screening tools (risk assessment + FPG and A1C)
  - Type 2 diabetes is preventable!
    - ~1/3 of diabetes undiagnosed with complications present at baseline



Harris MI. *Consultant* 1997;37(suppl):S9

# Diabetes Screening and Diagnosis

## ADA Criteria – Testing in Asymptomatic Adults

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Testing should be considered in all adults who are overweight (BMI  $\geq 25$ ) and have additional risk factors:

- Family history of diabetes (1st degree relative)
- High risk ethnic populations group (NA, Asian Am, Latino, AA/API)
- Chronic health conditions (CVD , hypertension, dyslipidemia)
- Prior history of elevated blood glucose or A1C
- History of gestational diabetes or child > 9 lbs at birth
- Other conditions associated with insulin resistance
  - Morbid obesity, polycystic ovarian syndrome (PCOS), acanthosis

*In the absence of risk factors, testing should begin at age 45 years. If normal, testing should be repeated at least every 3 years in a clinic setting*

American Diabetes Association. Standards of Medical Care in Diabetes – 2011 *Diabetes Care* 34; Suppl 1, 2011

# Prevention of Type 2 Diabetes

## Impact of Selected Interventions

### Lifestyle

Study		N	Intervention	Treatment	Risk Reduction
Da Qing	IGT	577	Lifestyle	6 years	-34 - 69%
Finnish DPS	IGT	523	Lifestyle	3+ years	-58%
DPP	IGT	3324	Lifestyle	3 years	-58%

### Pharmacologic

Study		N	Intervention	Treatment	Risk Reduction
DPP	IGT	3324	Metformin	3 years	-31%
IDPP	IGT	531	Metformin	3 years	-26%
STOP-NIDDM	IGT	1429	Acarbose	3 years	-21%
ACT NOW	IFG	~600	Pioglitazone	3 years	-81%
XENDOS	IGT	3305	Orlistat	4 years	-45%
DREAM	IGT	5269	Rosiglitazone	3 years	-60%

Pan XR. *Diabetes Care* 20:537-44, 1997. Tuomilehto J. *N Engl J Med* 344:1343-50, 2002

DPP Research Group. *N Engl J Med* 346:393-403, 2002. Ramachandran A. *Diabetologia* 49:289, 2006

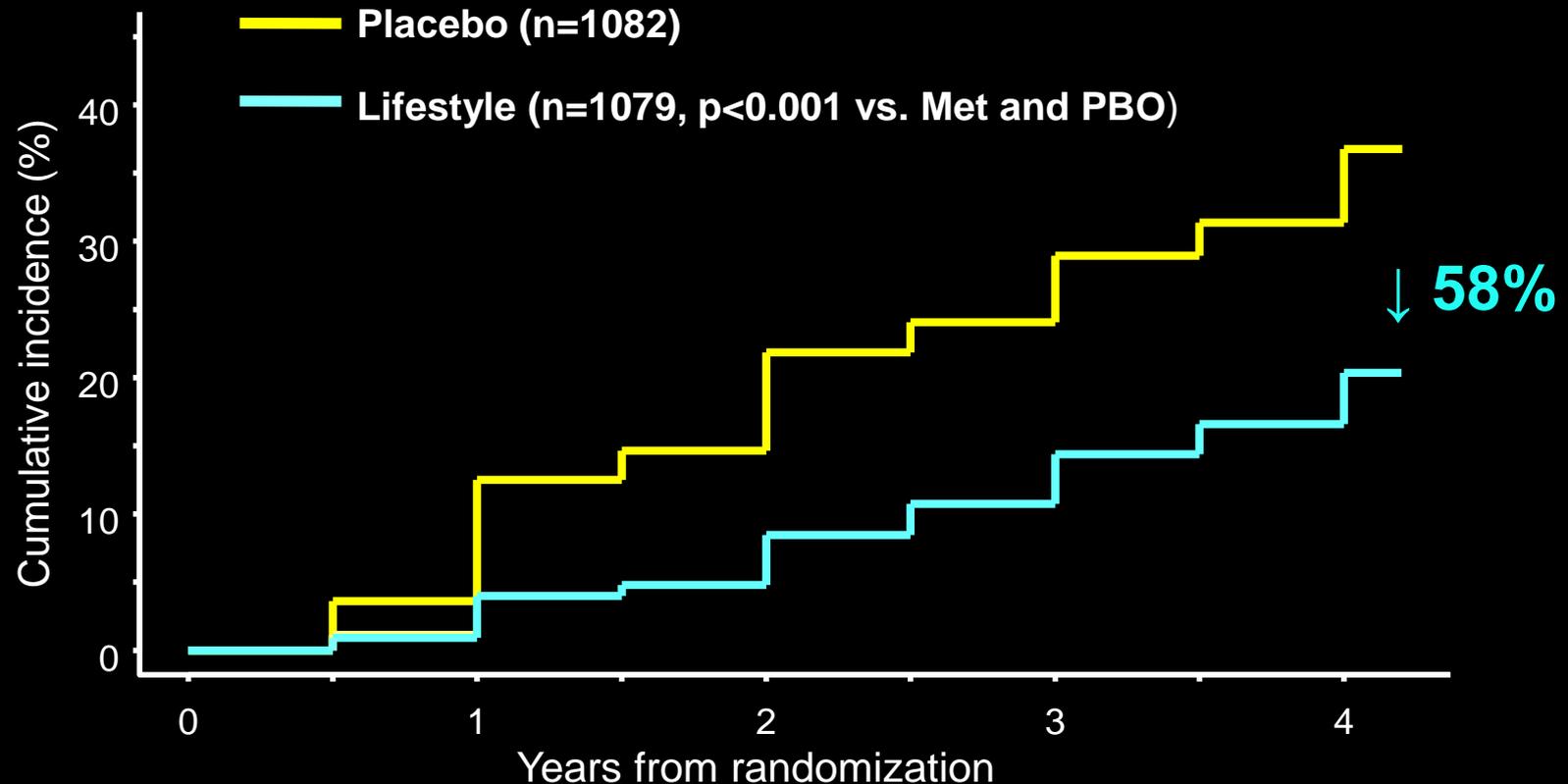
Holman RR. *Diabetic Medicine* 20(Suppl. 2): 15, 2003. Torgerson JS, et al. *Diabetes Care*. 2004;27:155-161

Chiasson JL. *Lancet*. 2002 Jun 15;359(9323):2072-7. DREAM Trial Investigators. *Lancet*. 2006;368:1096-1105.

DeFronzo RA, et al. ADA 68th Scientific Sessions 2008. ORIGIN Trial Investigators. *Am Heart J* 2008;155:26-32.

# Diabetes Prevention Program (DPP) Prevention of Diabetes

Percent developing diabetes



The DPP Research Group, *NEJM* 346:393-403, 2002

# Prevention Of Type 2 Diabetes 2020: Impact of Lifestyle Interventions

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- Lifestyle therapy = very effective in preventing or delaying the onset of type 2 diabetes in those at highest risk
  - Family history
  - IFG and IGT
- The lifestyle therapy that works involves three core features

Balanced low-calorie nutrition

Regular physical activity

Frequent intervention and support

Broadly integrated into community programs

# Diabetes Prevention Lifestyle Program

## A Working Example – U.S. YMCA

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Treating 100 high risk adults (age 50) for 3 years...

- Lay based education and support based on DPP
- Prevents 15 new cases of Type 2 Diabetes<sup>1</sup>

Impact on direct and indirect costs

- Prevents 162 missed work days<sup>2</sup>
- Avoids the need for BP/Chol pills in 11 people<sup>3</sup>
- Avoids \$91,400 in healthcare costs<sup>4</sup>
- Adds the equivalent of 20 perfect years of health<sup>5</sup>

1 DPP Research Group. N Engl J Med. 2002 Feb 7;346(6):393-403

2 DPP Research Group. Diabetes Care. 2003 Sep;26(9):2693-4

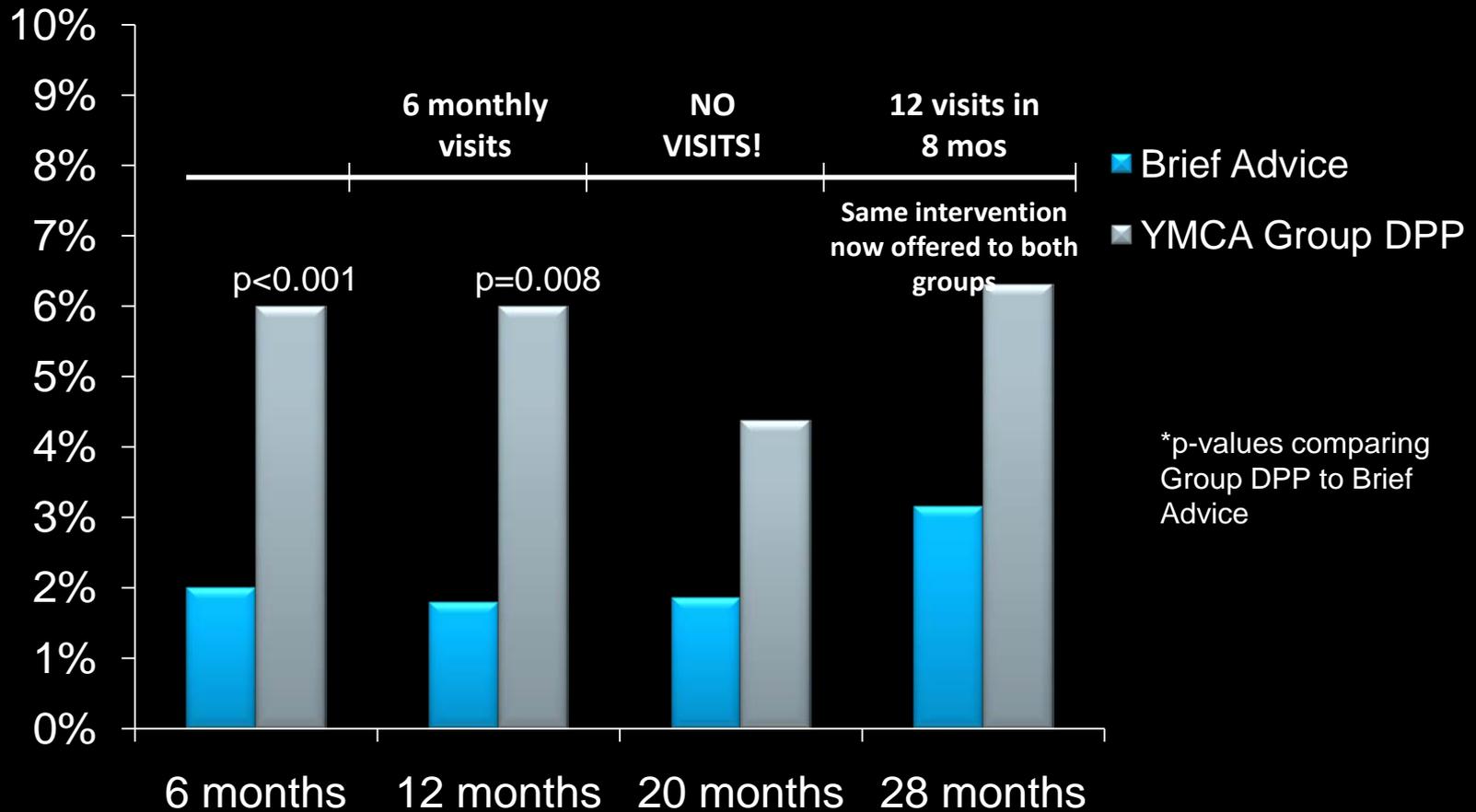
3 Ratner, et al. 2005 Diabetes Care 28 (4), pp. 888-894

4 Ackermann, et al. 2008 Am J Prev Med 35 (4), pp. 357-363; estimates scaled to 2008 \$US

5 Herman, et al. 2005 Ann Intern Med 142 (5), pp. 323-32

# DEPLOY Weight Reduction & Maintenance

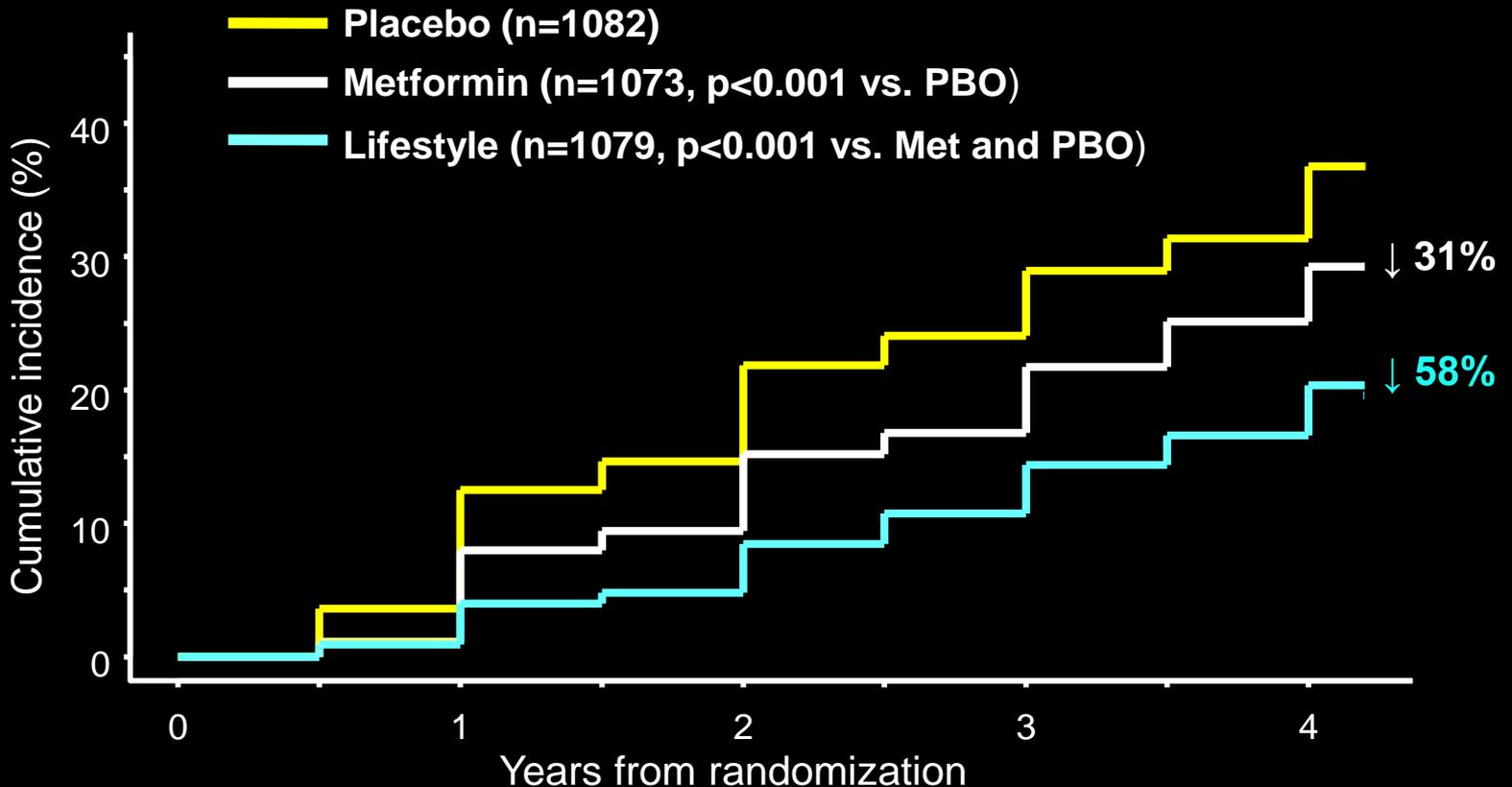
## Low Cost Lay Program for Diabetes Prevention



Ackermann, et al. Am J Prev Med. 2008 Oct;35(4):357-63; Long term results under review 06/2010

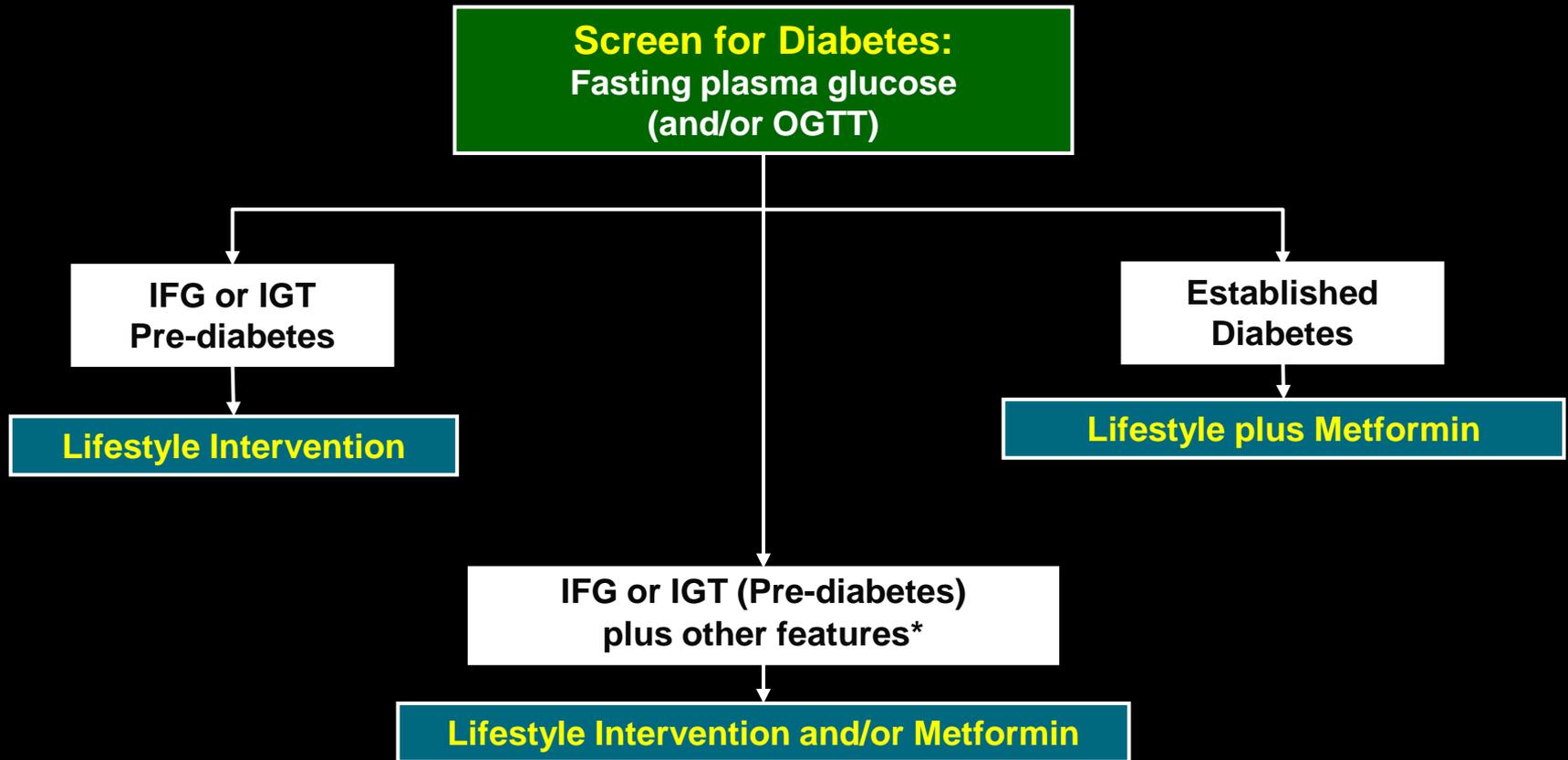
# Diabetes Prevention Program (DPP) Prevention of Diabetes

Percent developing diabetes



The DPP Research Group, *NEJM* 346:393-403, 2002

# A Practical Approach to Pre-Diabetes and Diabetes Prevention



Adapted from Nathan DM, et al. *Diabetes Care* 2007; 30:753-759. Nathan DM, et al. *Diabetes Care* 2008; 31:173-175. ADA. *Diabetes Care* 2008; 31:s12-s54.

# Prevention Of Type 2 Diabetes 2020: Impact of Lifestyle Interventions

---

- Lifestyle therapy = effective in preventing or delaying the onset of type 2 diabetes in those at highest risk:
  - Family history
  - IFG and IGT
- The lifestyle therapy that works involves three core features:

Balanced low-calorie nutrition

Regular physical activity

Frequent intervention and support

- Broadly integrated into community programs

# Standards of Care – 2011 and Beyond

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- **Diabetes and pre-diabetes awareness**
  - Risk assessment
  - Screening and detection (increased use of A1C!)
- **Application of early intensive therapy**
  - Non-pharmacologic and pharmacologic
- **Research and discovery**
  - Diabetes prediction
  - Complications prediction, prevention and regression

# Resources - ADA

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- Stop the Diabetes Movement
- Awakening the Spirit
- Clinician Support Tools
  - Estimated average glucose
  - Professional website resources
  - ADA website – general diabetes information
- Living with Type 2 - new patient initiative

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“The intuitive mind is a sacred gift and the rational mind a faithful servant.

We will have created a society that honors the servant and has forgotten the gift if we are not careful.”

Thank You.