Diabetes Update
New Insulins
and
Insulin Delivery Systems

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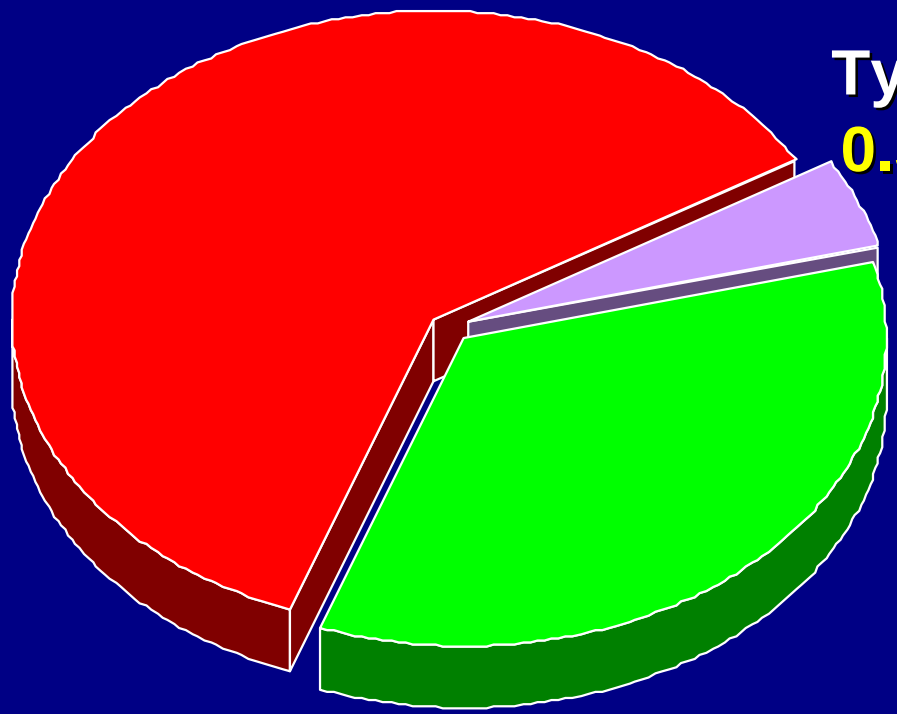
Atlanta, Georgia

Prevalence of Diabetes in the US

Diagnosed Type 2 Diabetes 10.3 Million

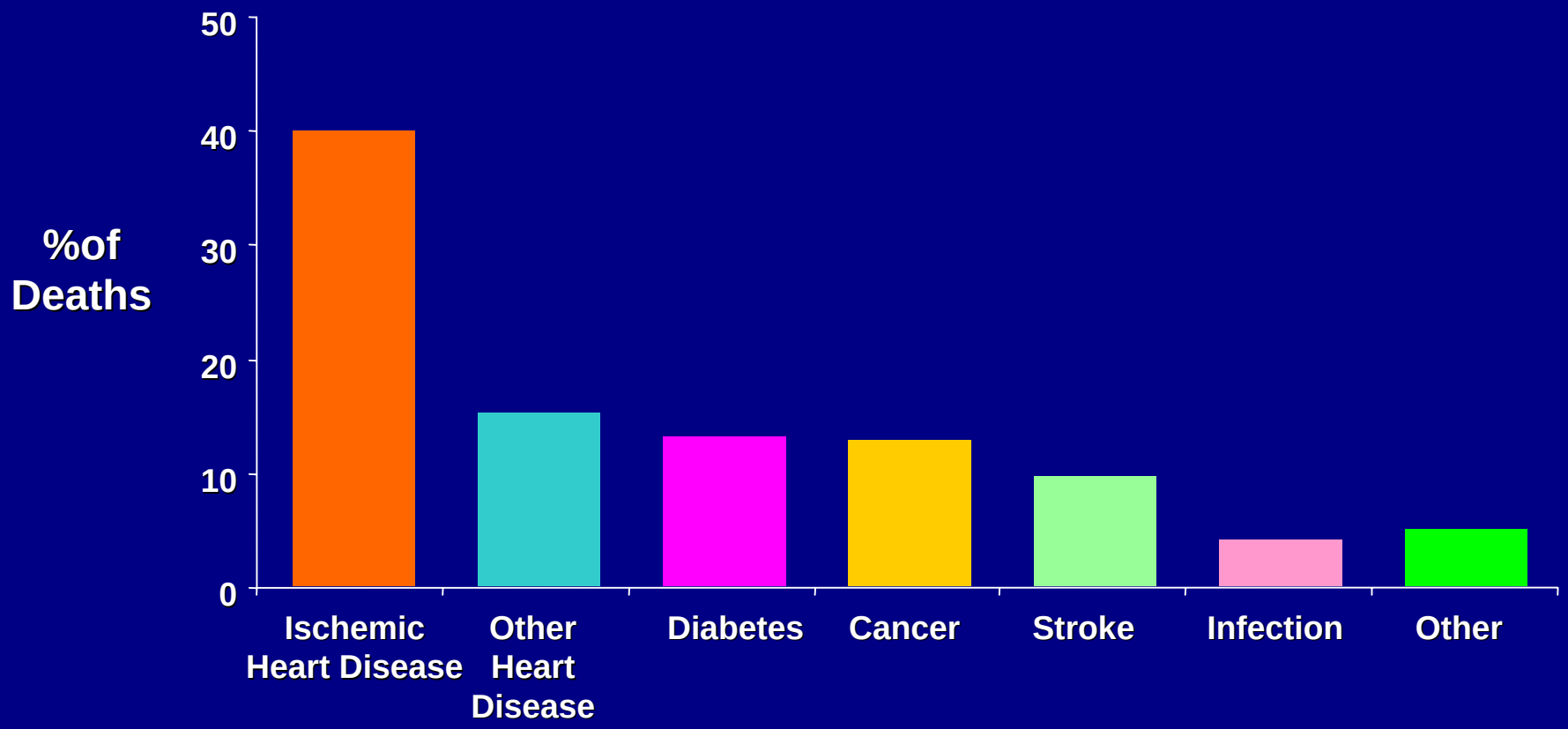


Diagnosed Type 1 Diabetes 0.5 – 1.0 Million

Undiagnosed Diabetes 5.4 Million

American Diabetes Association. Facts and Figures. Available at: http://www.diabetes.org/ada/facts.asp. Accessed January 18, 2000.

Causes of Death in People With Diabetes



Geiss LS, et al. In: *Diabetes in America*, 2nd ed. 1995. Bethesda, MD: National Institutes of Health; 1995:chap 11.

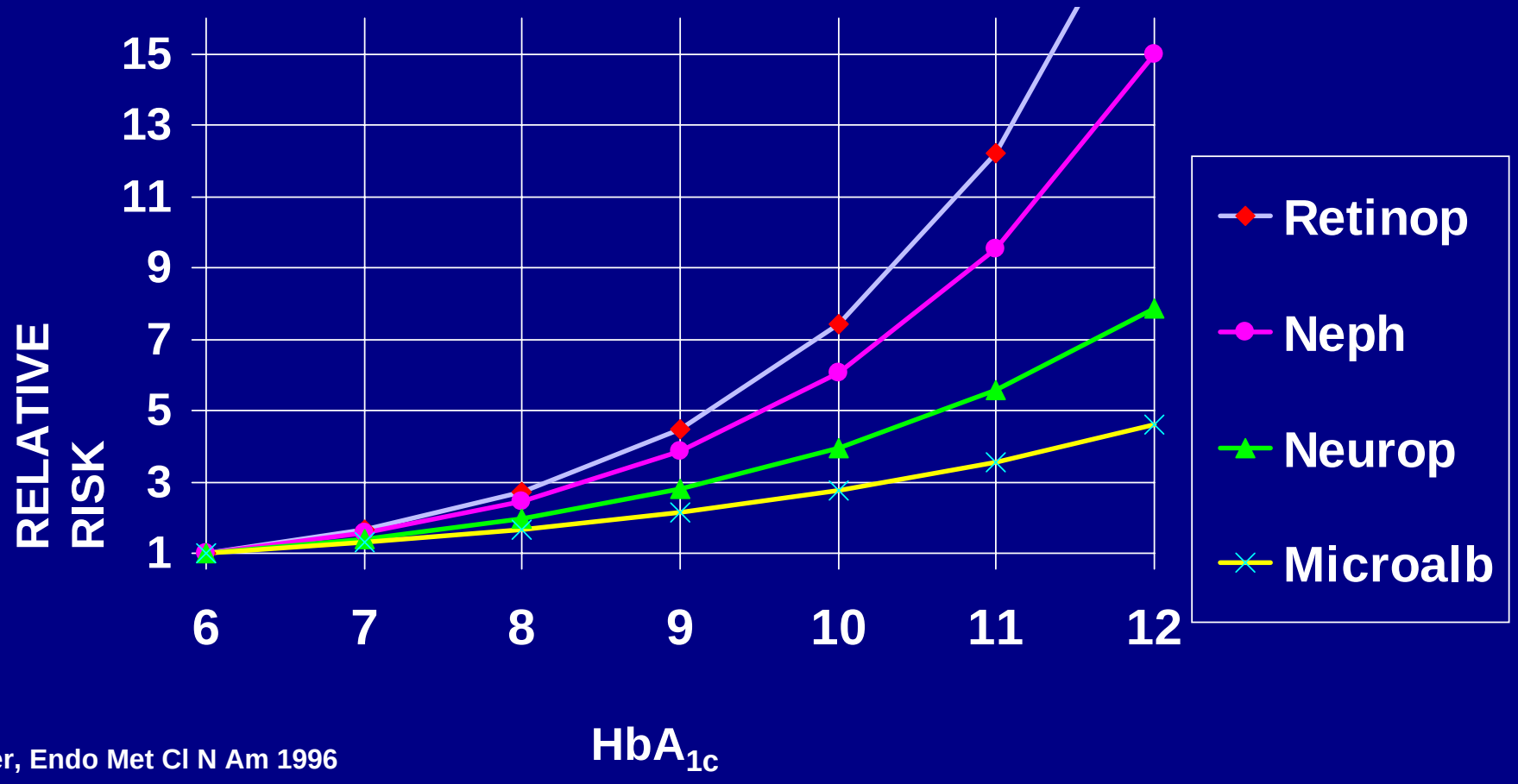
Goals of Intensive Diabetes Management

- Near-normal glycemia
  - HbA1c less than 6.5 to 7.0%
- Avoid short-term crisis
  - Hypoglycemia
  - Hyperglycemia
  - DKA
- Minimize long-term complications
- Improve QOL

ADA: *Clinical Practice Recommendations*. 2001.

Relative Risk of Progression of Diabetic Complications by Mean HbA1C

Based on DCCT Data



Skyler, Endo Met Cl N Am 1996

HbA1c and Plasma Glucose

- 26,056 data points (A1c and 7-point glucose profiles) from the DCCT
- Mean plasma glucose = (A1c x 35.6) – 77.3
- Post-lunch, pre-dinner, post-dinner, and bedtime correlated better with A1c than fasting, post-breakfast, or pre-lunch

Rohlfing et al, Diabetes Care 25 (2) Feb 2002

Emerging Concepts

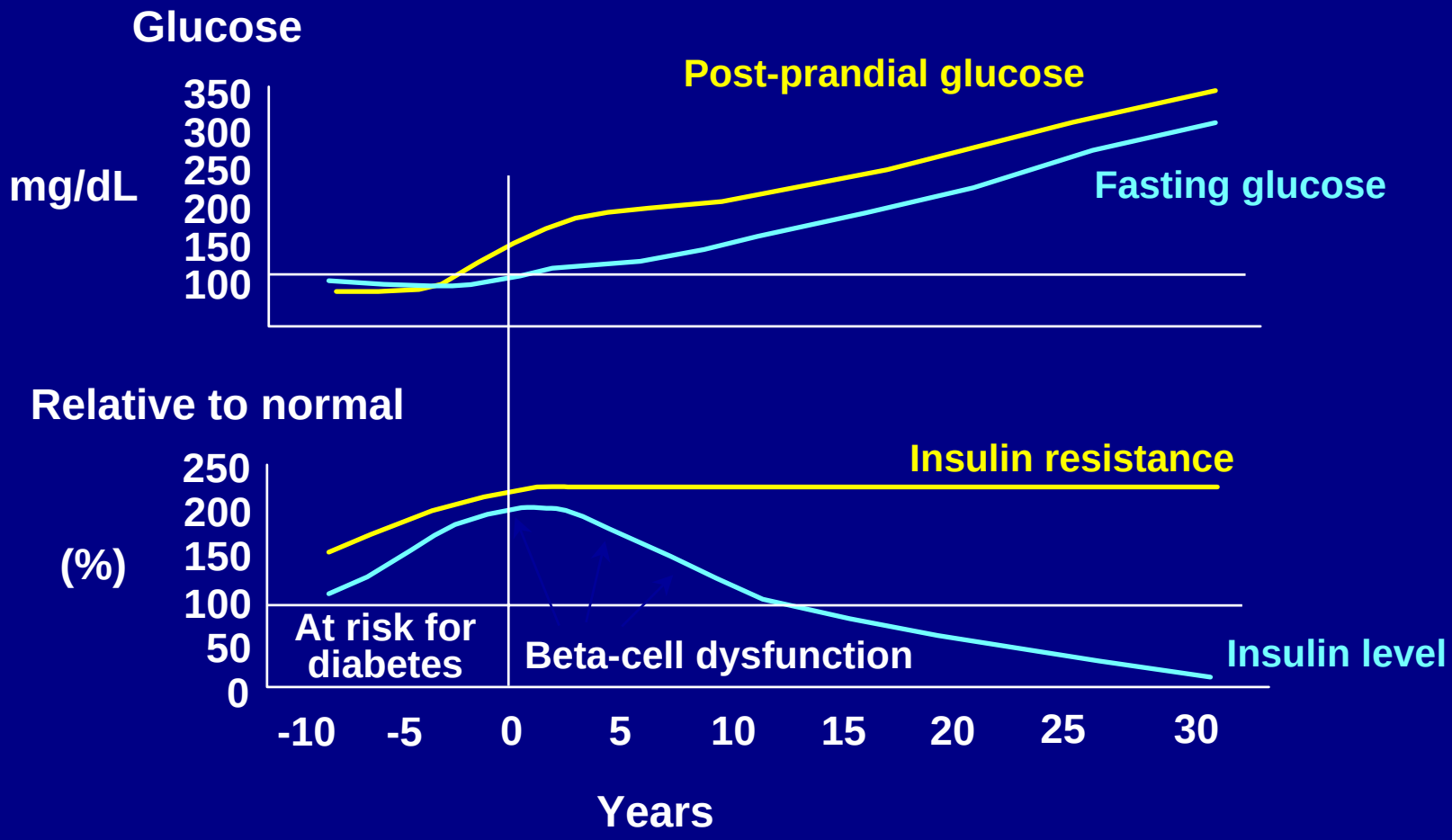
The Importance of Controlling Postprandial Glucose

ACE / AACE Targets for Glycemic Control

HbA_{1c}	< 6.5 %
Fasting/preprandial glucose	< 110 mg/dL
Postprandial glucose	< 140 mg/dL

ACE / AACE Consensus Conference, Washington DC August 2001

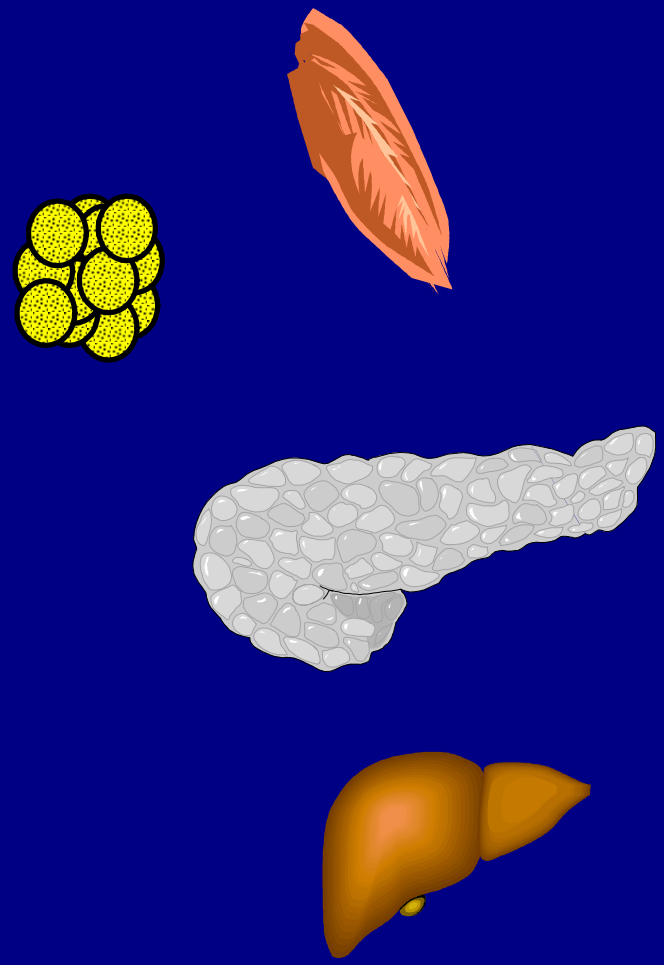
Natural History of Type 2 Diabetes



R.M. Bergenstal, International Diabetes Center

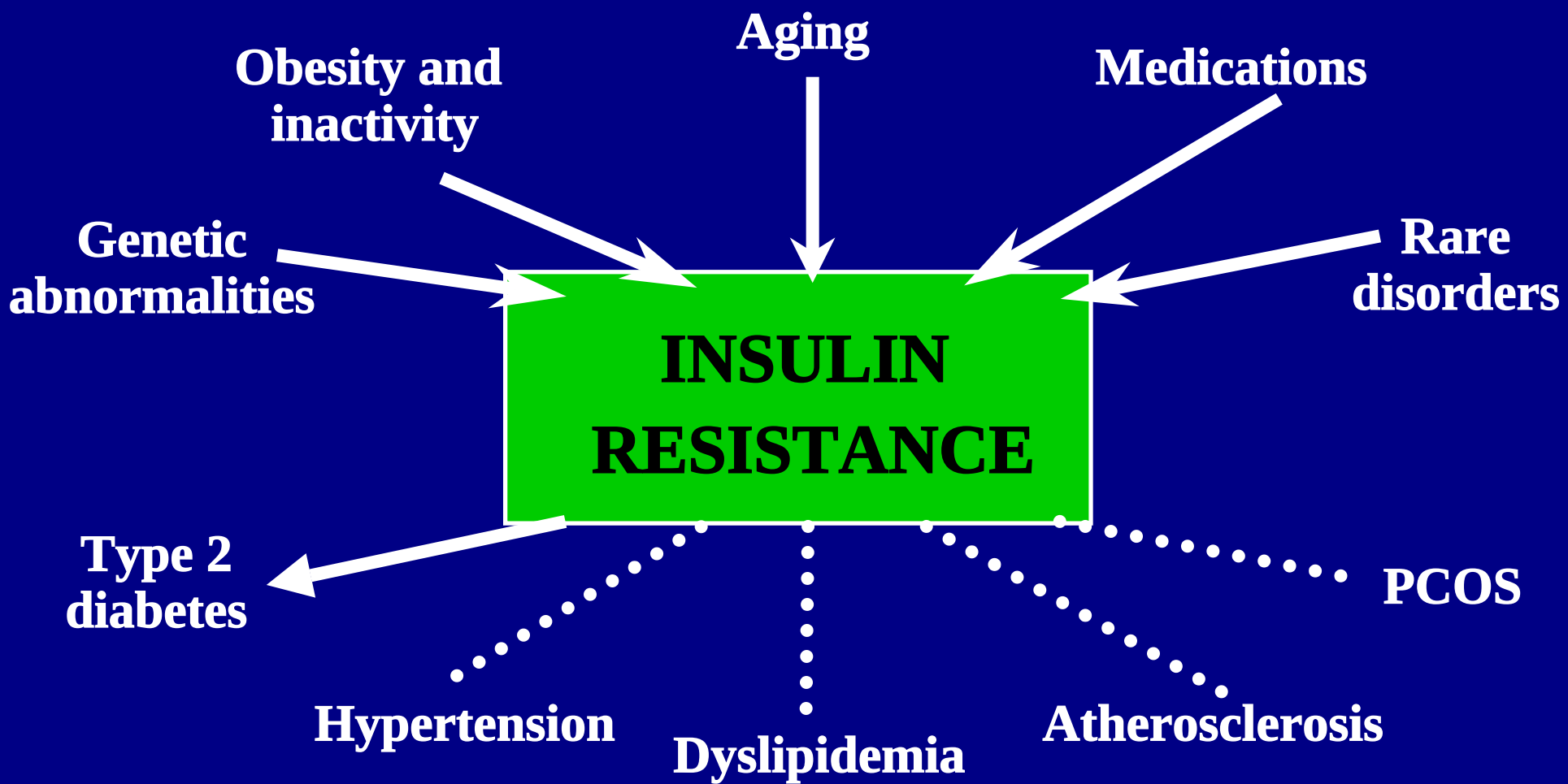
Major Metabolic Defects in Type 2 Diabetes

- Peripheral insulin resistance in muscle and fat
- Decreased pancreatic insulin secretion
- Increased hepatic glucose output



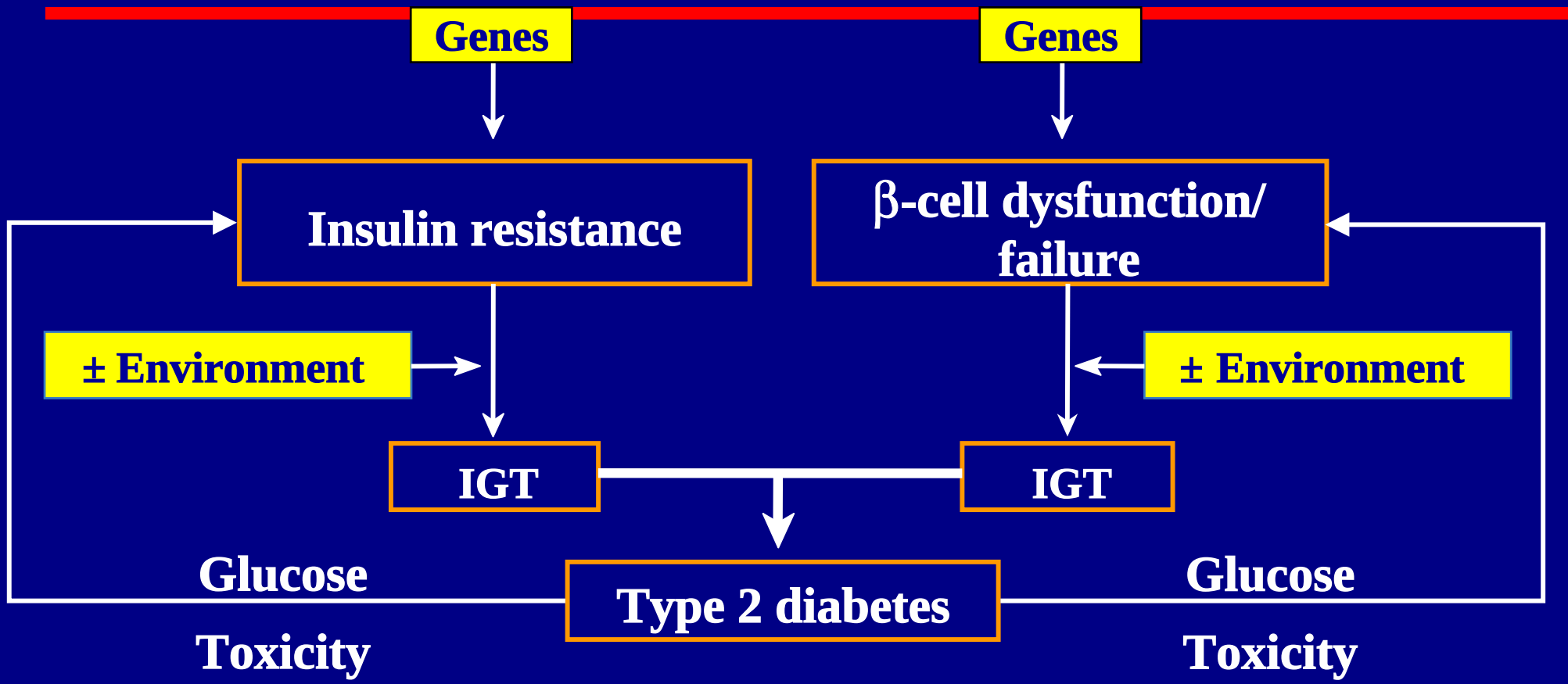
Haffner SM, et al. Diabetes Care, *1999*

Insulin Resistance: An Underlying Cause of Type 2 Diabetes



Reaven GM. *Physiol Rev.* 1995;75:473-486
Clauser, et al. *Horm Res.* 1992;38:5-12.

Type 2 Diabetes: Two Principal Defects



Reaven GM. *Physiol Rev.* 1995;75:473-486
Reaven GM. *Diabetes/Metabol Rev.* 1993;9(Suppl 1):5S-12S;
Polonsky KS. *Exp Clin Endocrinol Diabetes.* 1999;107 Suppl 4:S124-S127.

Role of Free Fatty Acids in Hyperglycemia

Adipose tissue insulin resistance

ADIPOSE TISSUE

↑ **Lipolysis**

↑ **FFA mobilization**

MUSCLE

Muscle insulin resistance

↑ **FFA oxidation**

↓ **Glucose utilization**

LIVER

Liver insulin resistance

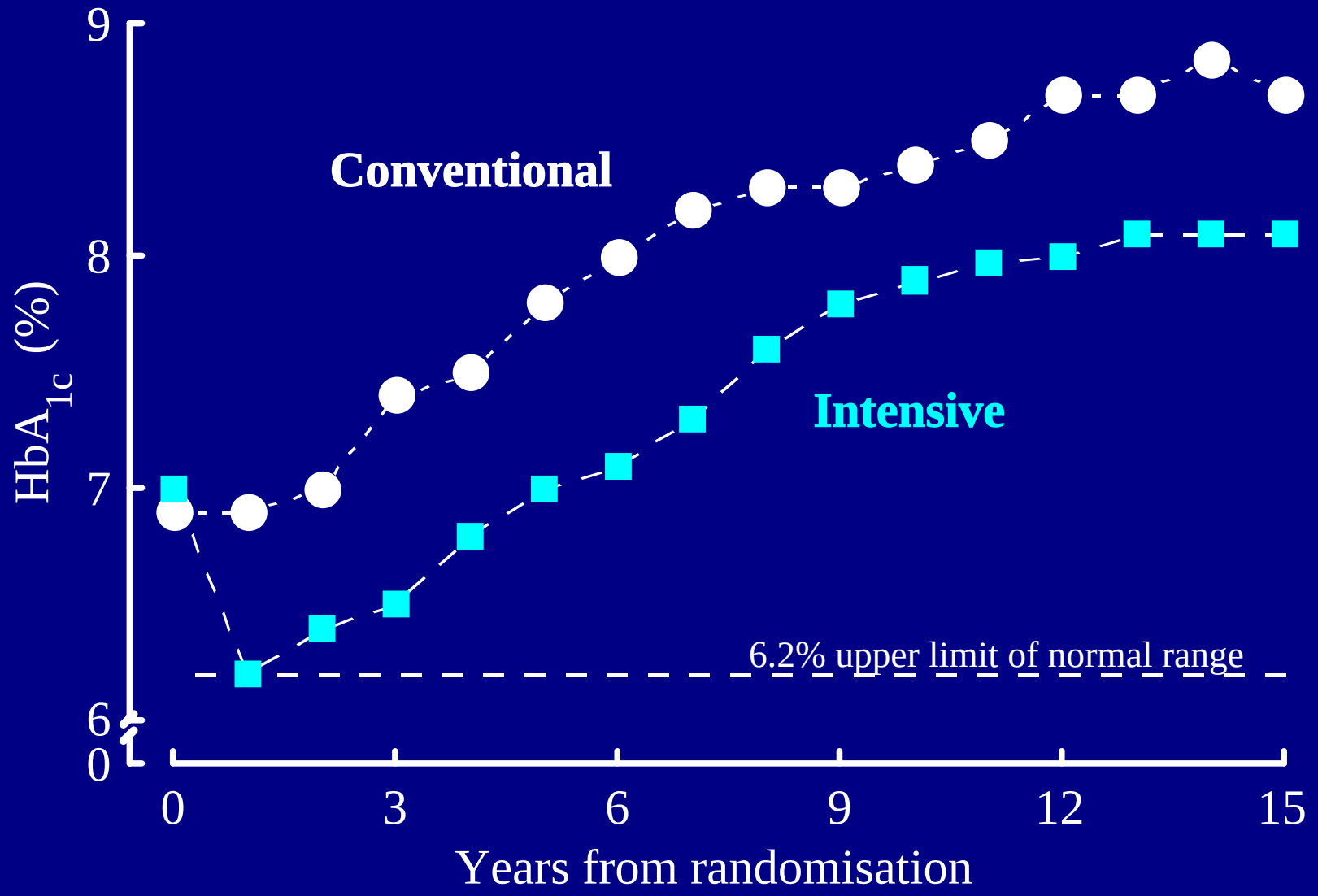
↑ **FFA oxidation**

↑ **Gluconeogenesis**

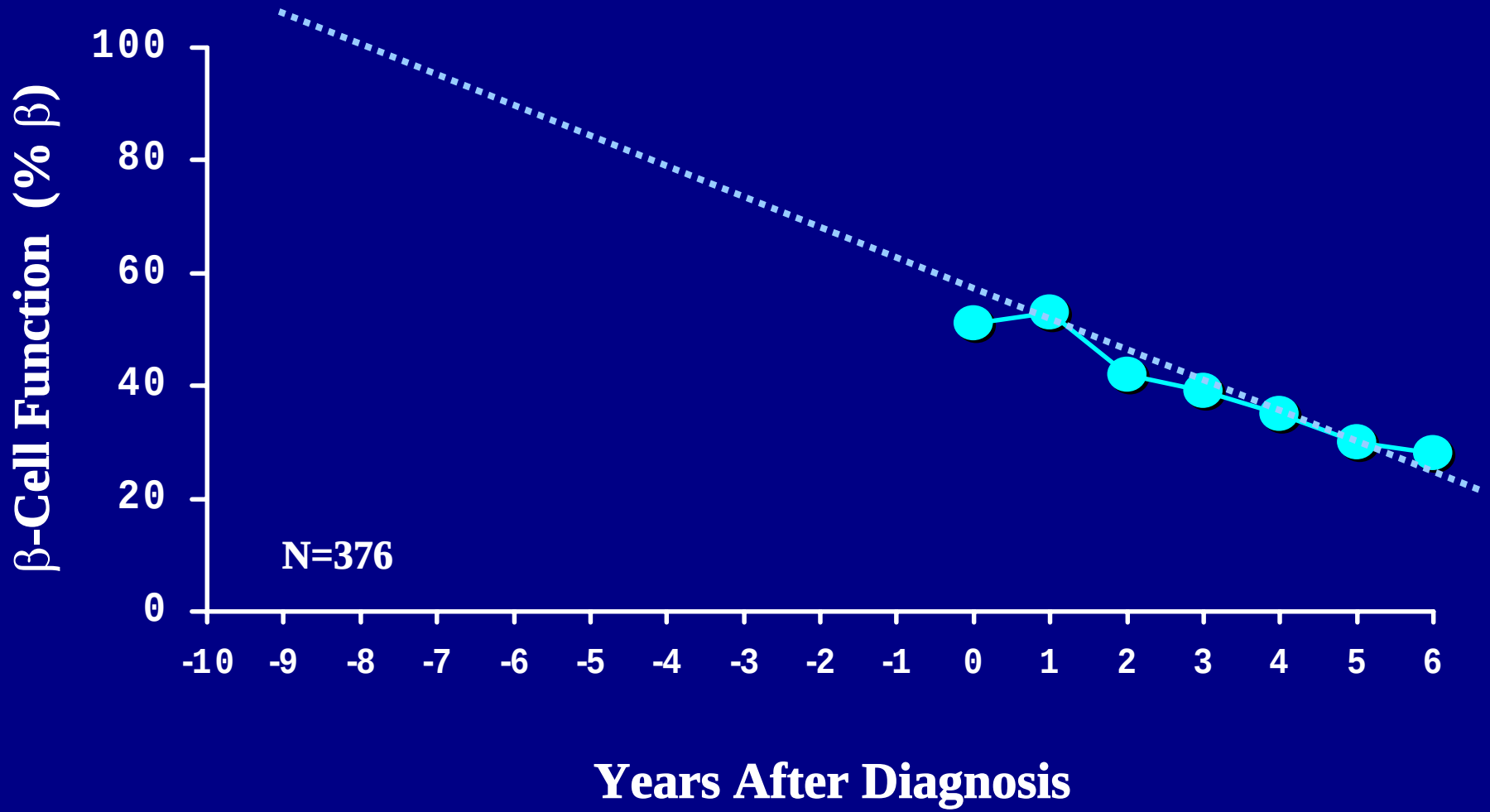
Hyperglycemia

Boden G. *Proc Assoc Am Physicians*. 1999;111:241-248.

HbA_{1c} in the UKPDS

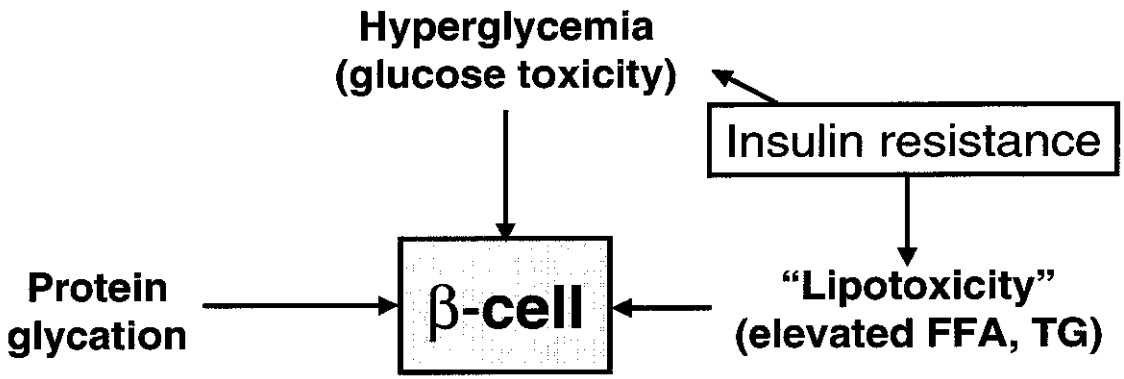


UKPDS: β-Cell Function for the Patients Remaining on Diet for 6 Years



Adapted from UKPDS Group. *Diabetes.* 1995; 44:1249-1258.

Multiple Factors May Drive Progressive Decline of β-Cell Function



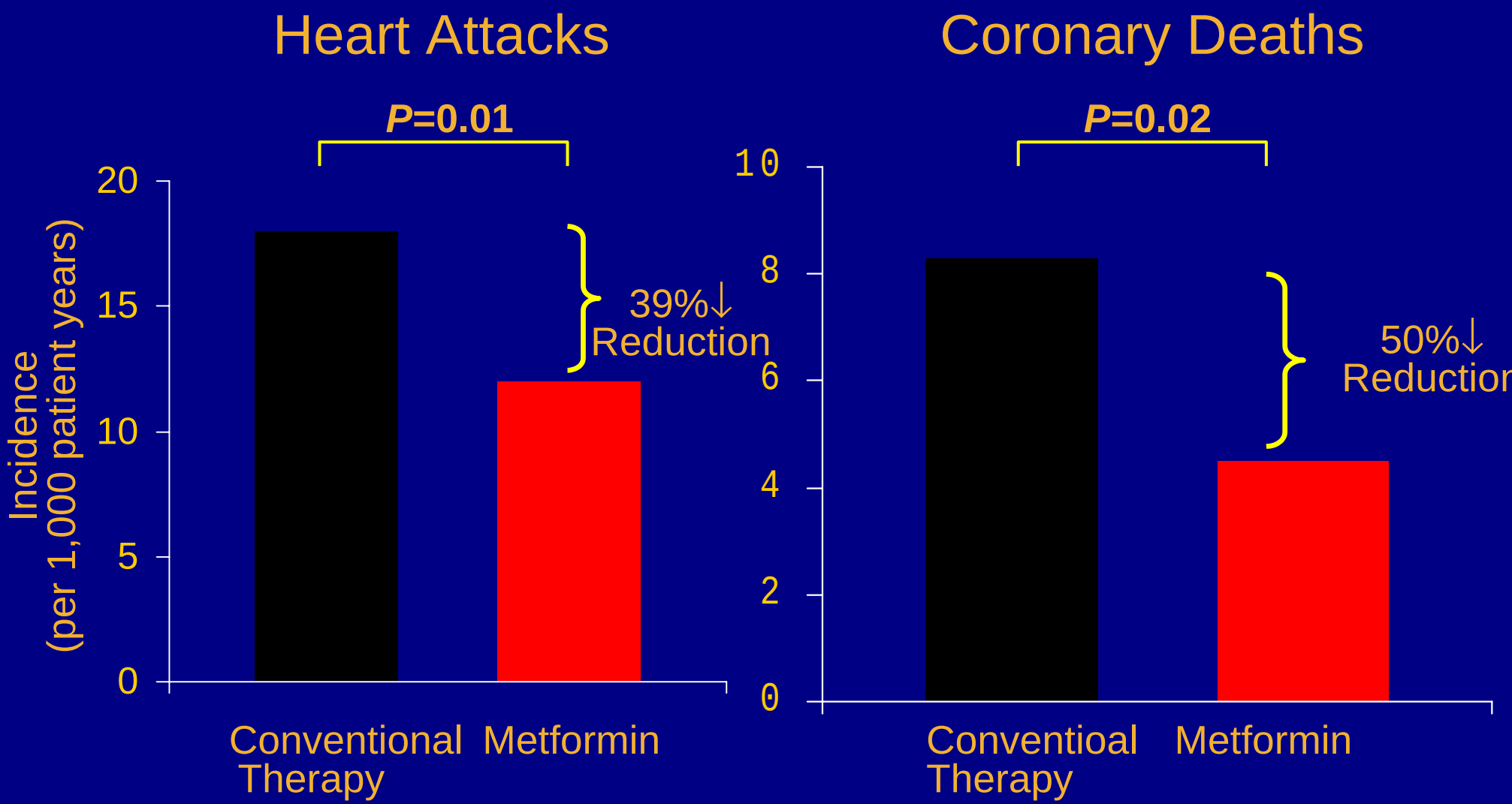
Reaven GM. *Physiol Rev*. 1995;73:473-486.

UKPDS: Benefits of Glycemic Control in Type 2 Diabetes

	Risk reduction over 10 years	
Any diabetes-related endpoint	12%	P = 0.029
Microvascular endpoints	25%	P = 0.0099
Myocardial infarction	16%	P = 0.052
Cataract extraction	24%	P = 0.046
Retinopathy at 12 years	21%	P = 0.015
Microalbuminuria at 12 years	33%	P < 0.001

UKPDS 33. *Lancet.* 1998;352:837-853.

Metformin Prevents Heart Attacks and Reduces Deaths in Type 2 Diabetes



Management of Type 2 DM Step Therapy

- Diet
- Exercise
- Sulfonylurea or Metformin
- Add Alternate Agent
- Add hs NPH vs TZD
- Switch to Mixed Insulin bid
- Switch to Multiple Dose Insulin

Utilitarian, Common Sense, Recommended

Prone to Failure from Misscheduling and Mismanagement

Management of Type 2 DM Stumble Therapy

- WAG Diet
- Golf Cart Exercise
- Sample of the Week Medication
  - Interrupted
  - Not Combined
- Poor Understanding of Goals
- Poor Monitoring

HbA1c >8% (If Seen)

Consider A New Treatment Paradigm

- Treatment designed to correct the dual impairments
- Vigorous effort to meet glycemic targets
- Simultaneous rather than sequential therapy
- Combination therapy from the outset
- Early step-wise titrations to meet glycemic targets

Goals in Management of Type 2 Diabetes

- **Fasting BG < 110 mg/dL**
- **Post-meal < 140 mg/dL**
- **HbA1c < 6.5%**
- **Blood Pressure < 130/80**
- **LDL < 100 mg/dl**
- **HDL > 45 mg/dl**

Thiazolidinediones: Mode of Action

Peroxisome Proliferator-Activated Receptors

- PPARγ
  - Affects glucose, lipid and protein metabolism
- PPARα
  - Affects lipoprotein metabolism

    (some TZDs)

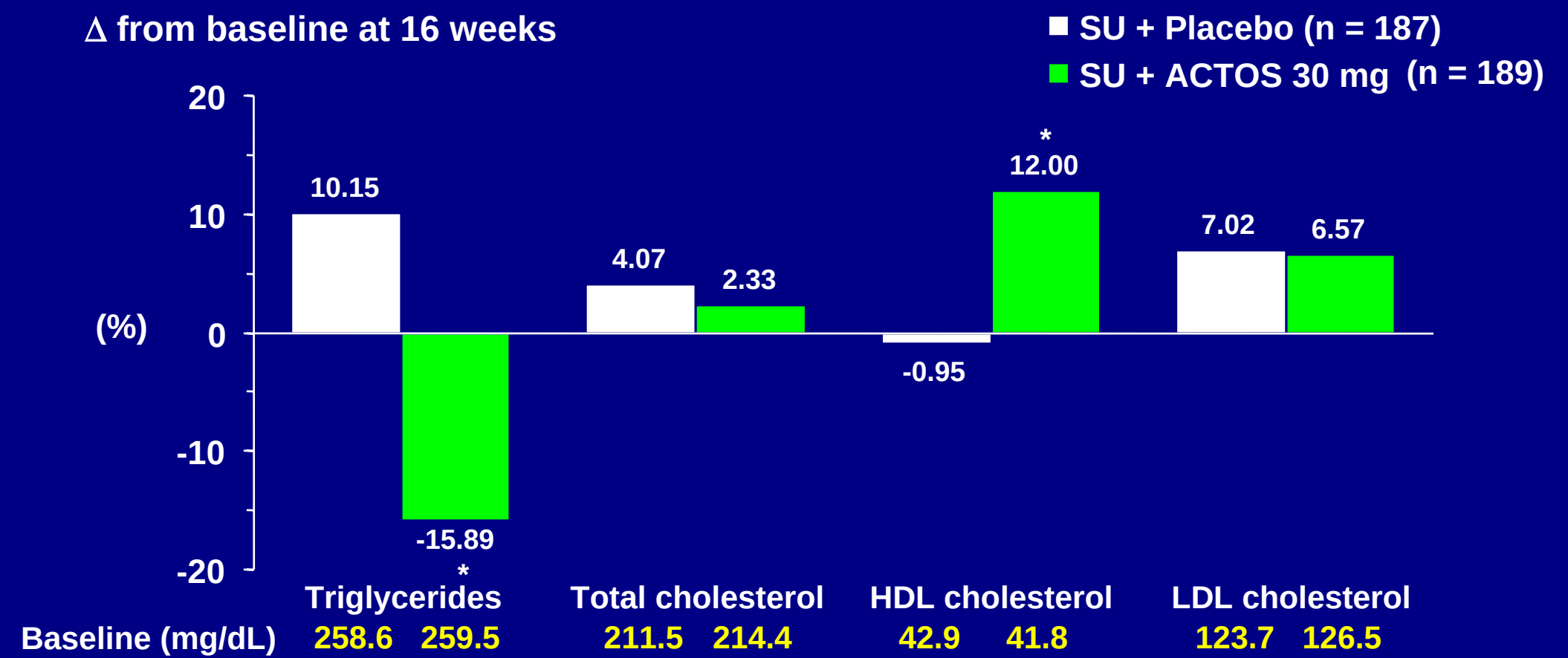
Saltiel & Olefsky. Diabetes *1996;45:1661–9*

Thiazolidinediones:
Rationale for Type 2 Diabetes Therapy

- Proven characteristics
  - Target insulin resistance, a core defect
  - Improve glycemic control
  - Do not cause hypoglycemia
  - Improve lipid profile (pioglitazone and troglitazone)
- Potential benefits
  - Preservation of pancreatic b-cell function
  - Prevention of progression from impaired glucose tolerance to type 2 diabetes
  - Improvement in cardiovascular outcomes

Saltiel & Olefsky. Diabetes *1996;45:1661–9*
Sonnenberg and Kotchen. Curr Opin Nephrol Hypertens *1998;7(5):551–5*

Change in Lipid Profile at Endpoint: ACTOS Added to Sulfonylurea

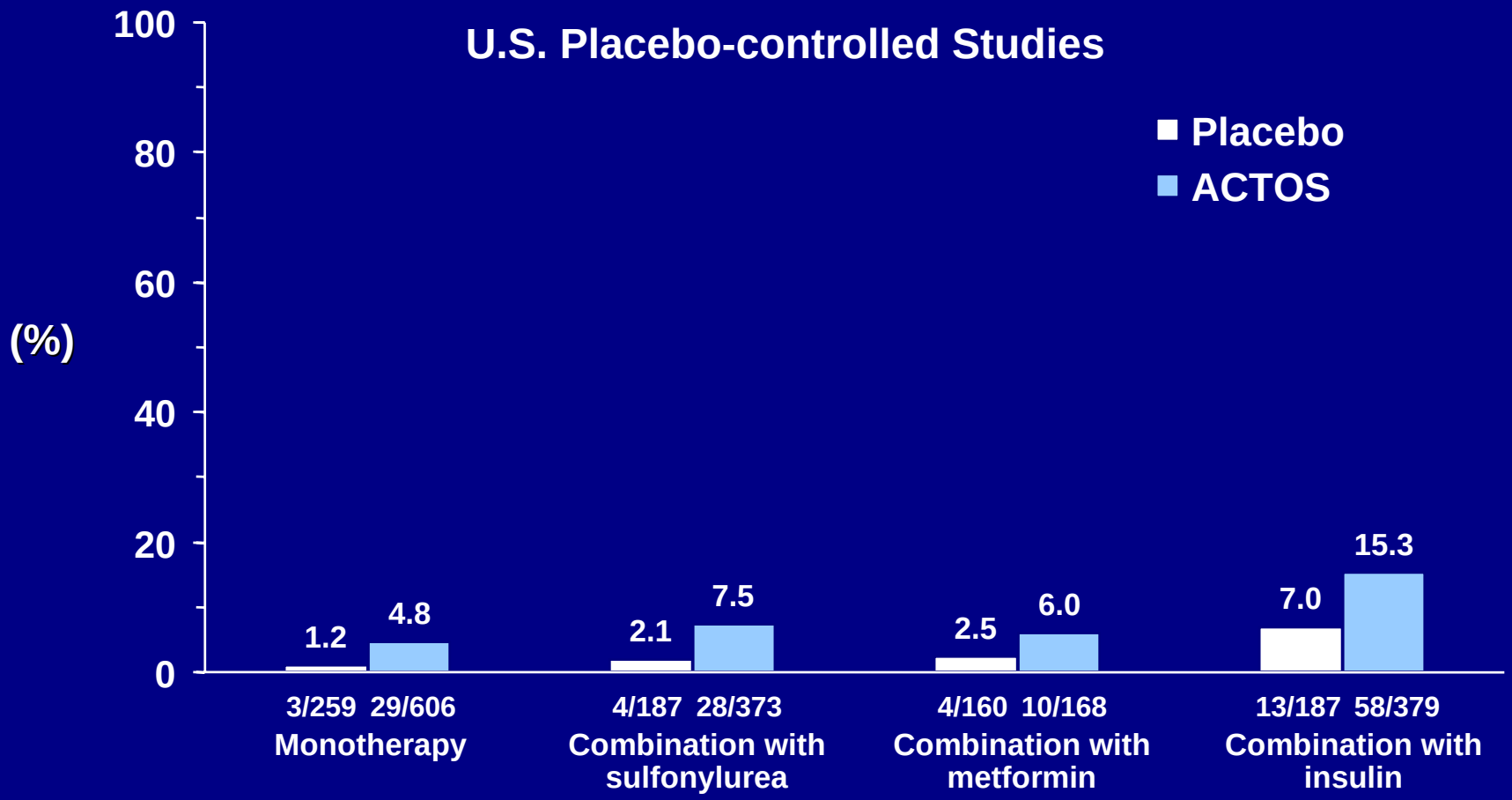


LOCF

* p≤ 0.05 vs. placebo

Takeda Pharmaceuticals America, Data on file Study 010

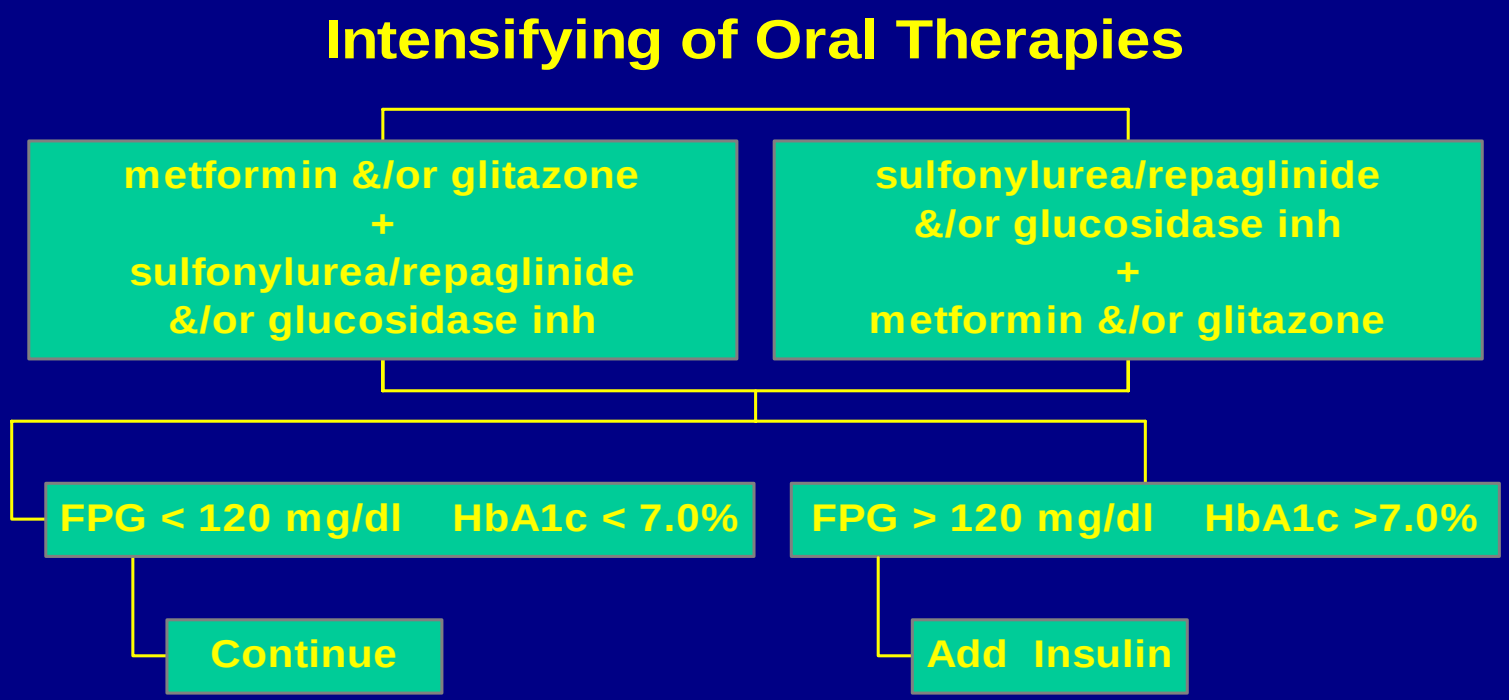
Incidence of Edema



2 patients from combination therapy trials and
0 from the monotherapy trials discontinued due to edema

Pioglitazone HCl Package Insert July, 1999

Approach to Combination Oral Therapy



Insulin

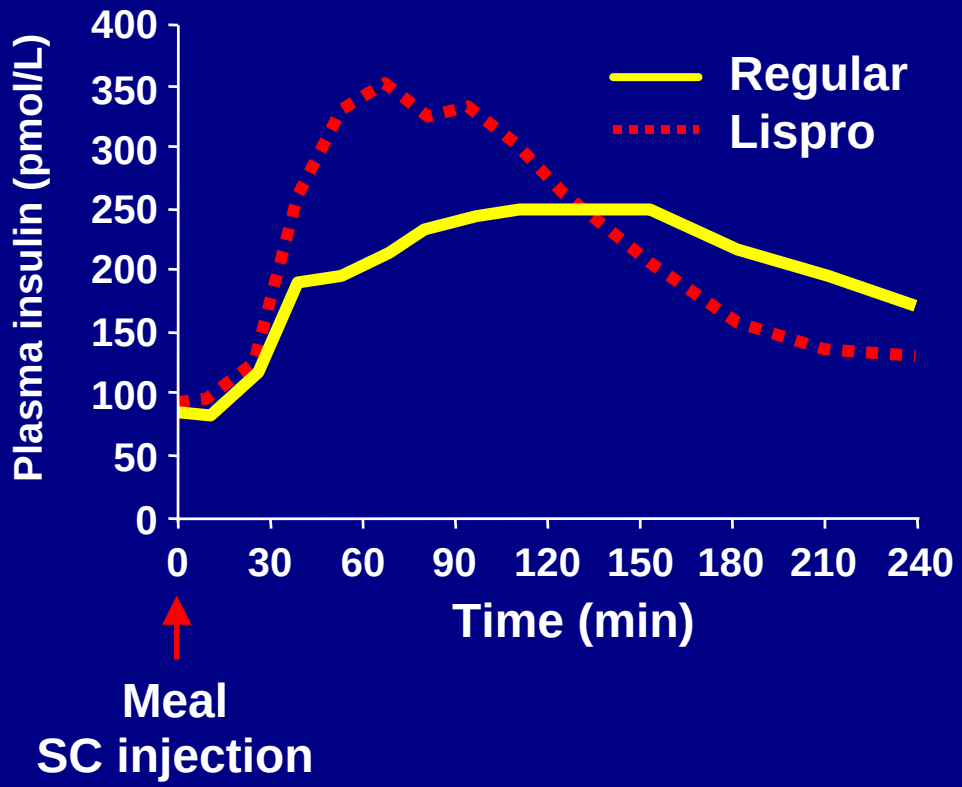
The most powerful agent we have to control glucose

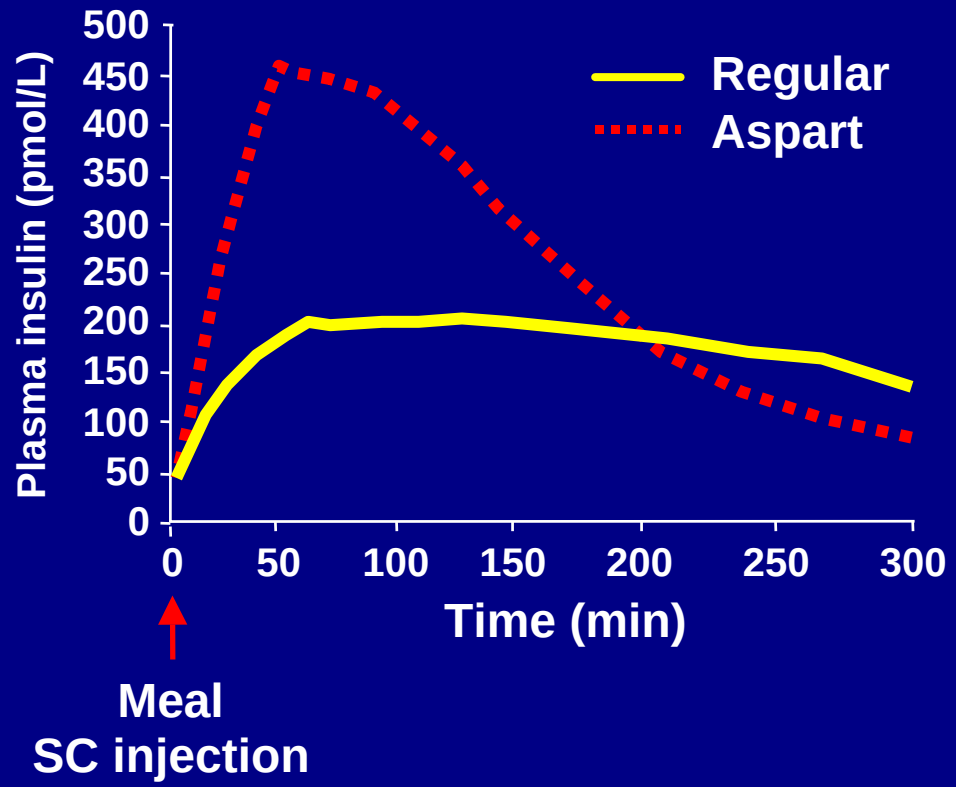
Comparison of Human Insulins / Analogues

Insulin preparations	Onset of action	Peak	Duration of action
Regular	30–60 min	2–4 h	6–10 h
NPH/Lente	1–2 h	4–8 h	10–20 h
Ultralente	2–4 h	Unpredictable	16–20 h
Lispro/aspart	5–15 min	1–2 h	4–6 h
Glargine	1–2 h	Flat	~24 h

Short-Acting Insulin Analogs

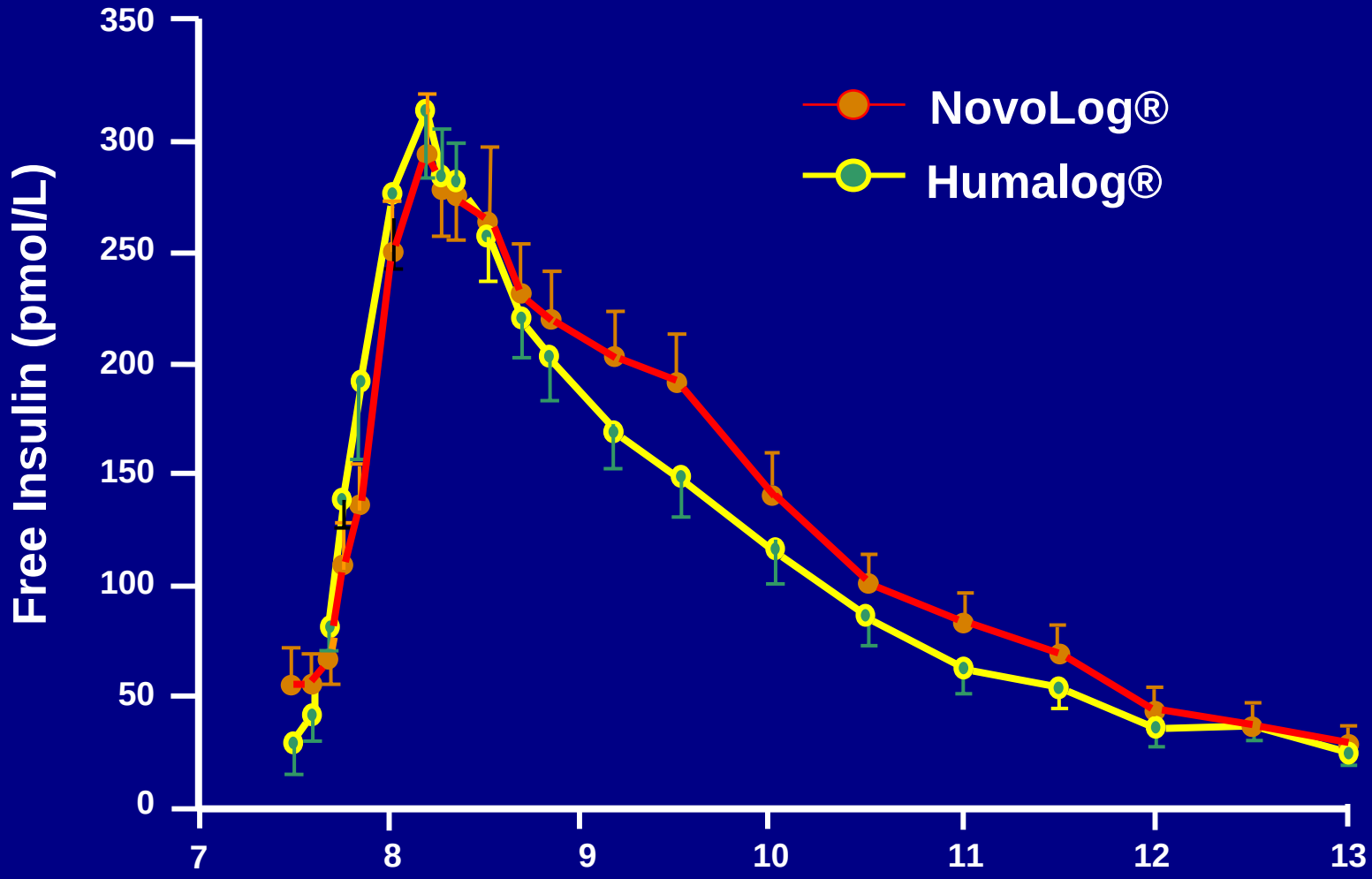
Lispro and Aspart Plasma Insulin Profiles





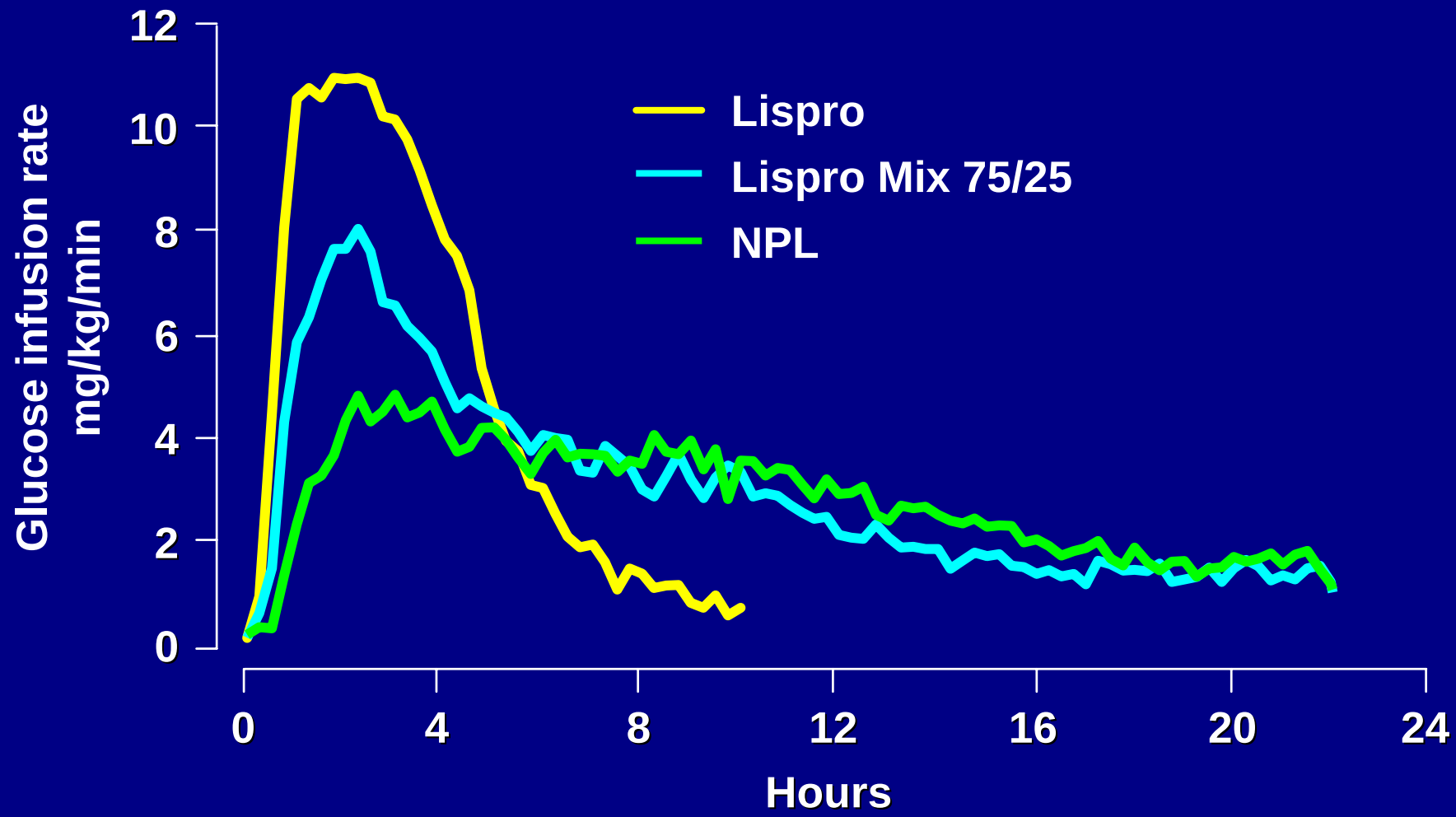
Heinemann, et al. *Diabet Med*. 1996;13:625–629; Mudaliar, et al. *Diabetes Care*. 1999;22:1501–1506.

Pharmacokinetic Comparison
NovoLog® *vs* Humalog®



Hedman, *Diabetes Care* 2001; 24(6):1120-21

Lispro Mix 75/25
Pharmacodynamics



Heise T, et al. *Diabetes Care*. 1998;21:800–803.

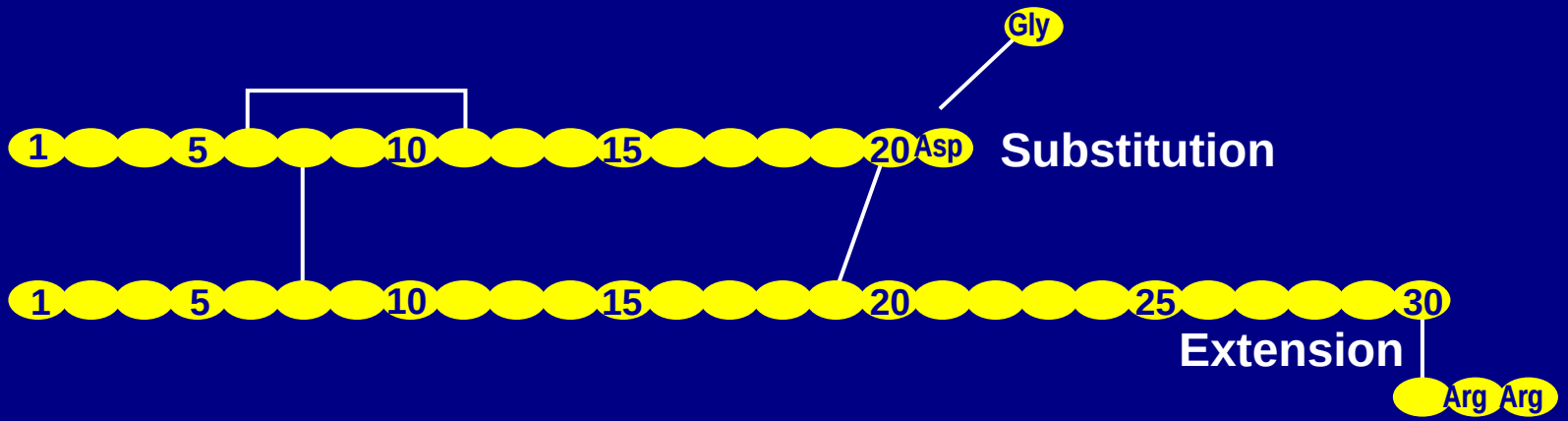
Limitations of NPH, Lente, and Ultralente

- Do not mimic basal insulin profile
  - Variable absorption
  - Pronounced peaks
  - Less than 24-hour duration of action
- Cause unpredictable hypoglycemia
  - Major factor limiting insulin adjustments
  - More weight gain

Insulin Glargine

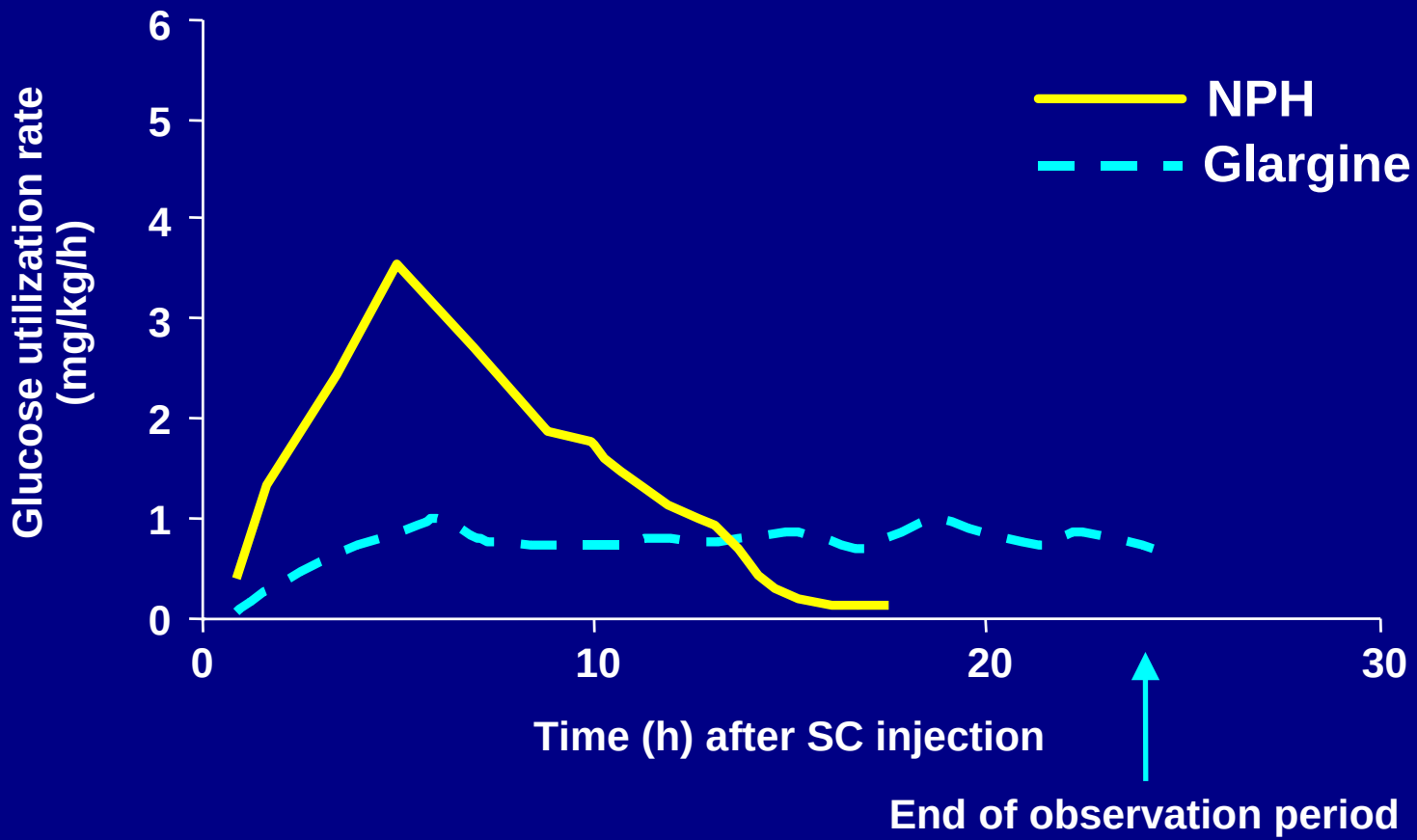
A New Long-Acting Insulin Analog

- Modifications to human insulin chain
  - Substitution of glycine at position A21
  - Addition of 2 arginines at position B30
- Gradual release from injection site
- Peakless, long-lasting insulin profile



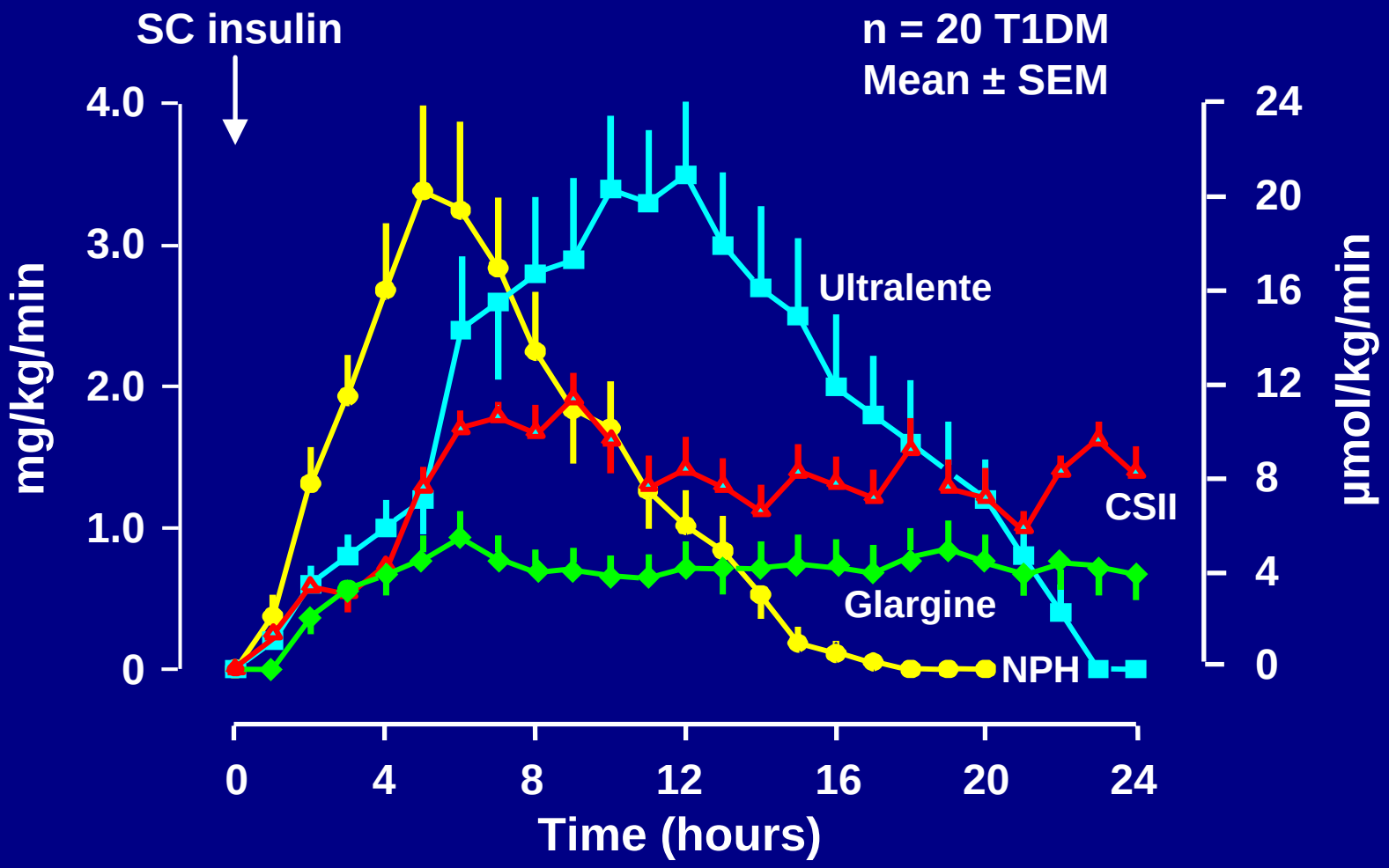
Glargine vs NPH Insulin in Type 1 Diabetes

Action Profiles by Glucose Clamp



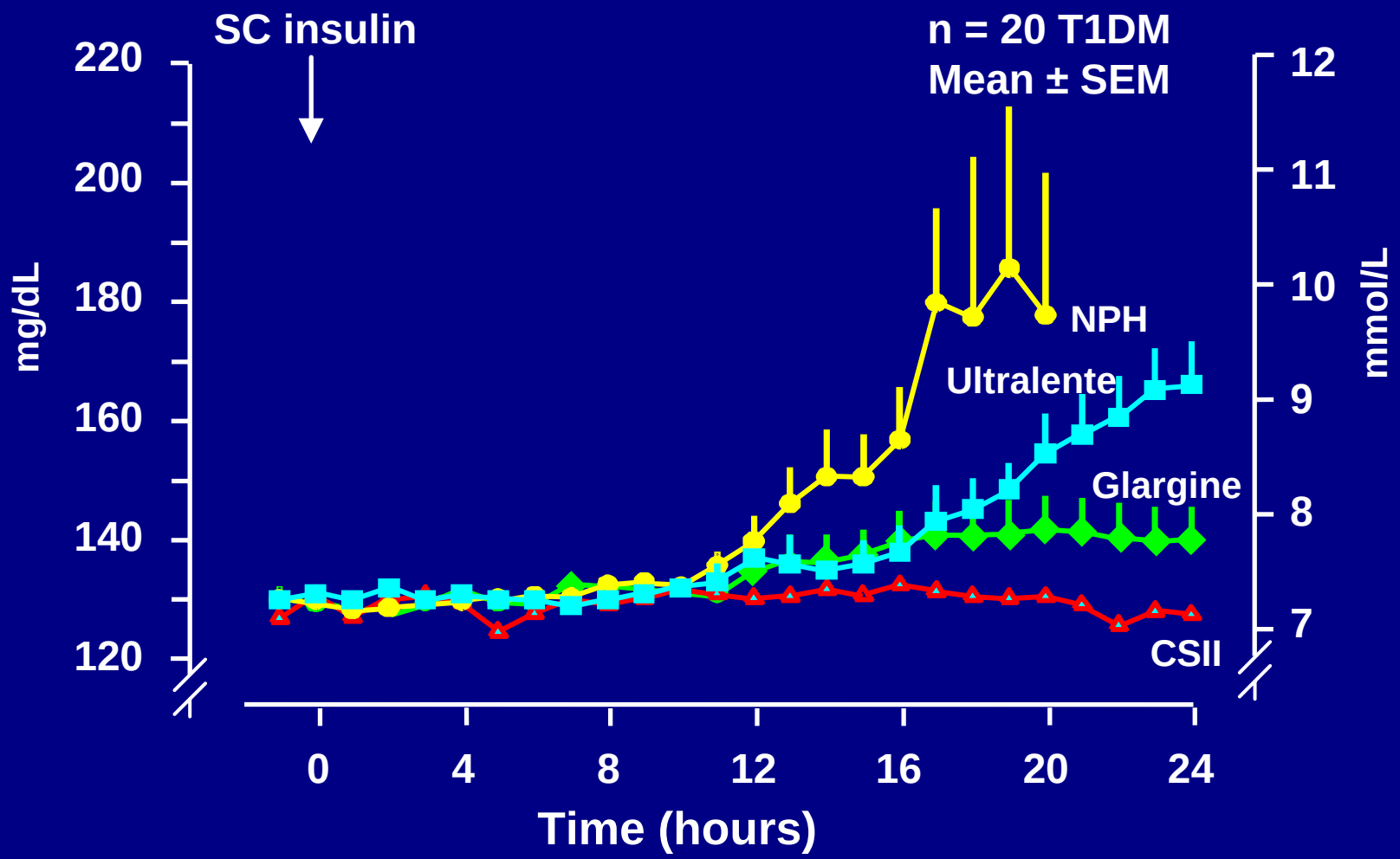
Lepore, et al. *Diabetes*. 1999;48(suppl 1):A97.

Glucose Infusion Rate



Lepore M, et al. *Diabetes*. 2000;49:2142–2148.

Plasma Glucose



Lepore M, et al. *Diabetes*. 2000;49:2142–2148.

Overall Summary: Glargine

- **Insulin glargine has the following clinical benefits**
  - **Once-daily dosing because of its prolonged duration of action and smooth, peakless time-action profile (*23.5 hours on repeat injections*)**
  - **Comparable or better glycemic control (FBG)**
  - **Lower risk of nocturnal hypoglycemic events**
  - **Safety profile similar to that of human insulin**

Type 2 Diabetes …
A Progressive Disease

Over time,
most patients will need insulin
to control glucose

Insulin Therapy in Type 2 Diabetes
Indications

- Significant hyperglycemia at presentation
- Hyperglycemia on maximal doses of oral agents
- Decompensation
  - Acute injury, stress, infection, myocardial ischemia
  - Severe hyperglycemia with ketonemia and/or ketonuria
  - Uncontrolled weight loss
  - Use of diabetogenic medications (eg, corticosteroids)
- Surgery
- Pregnancy
- Renal or hepatic disease

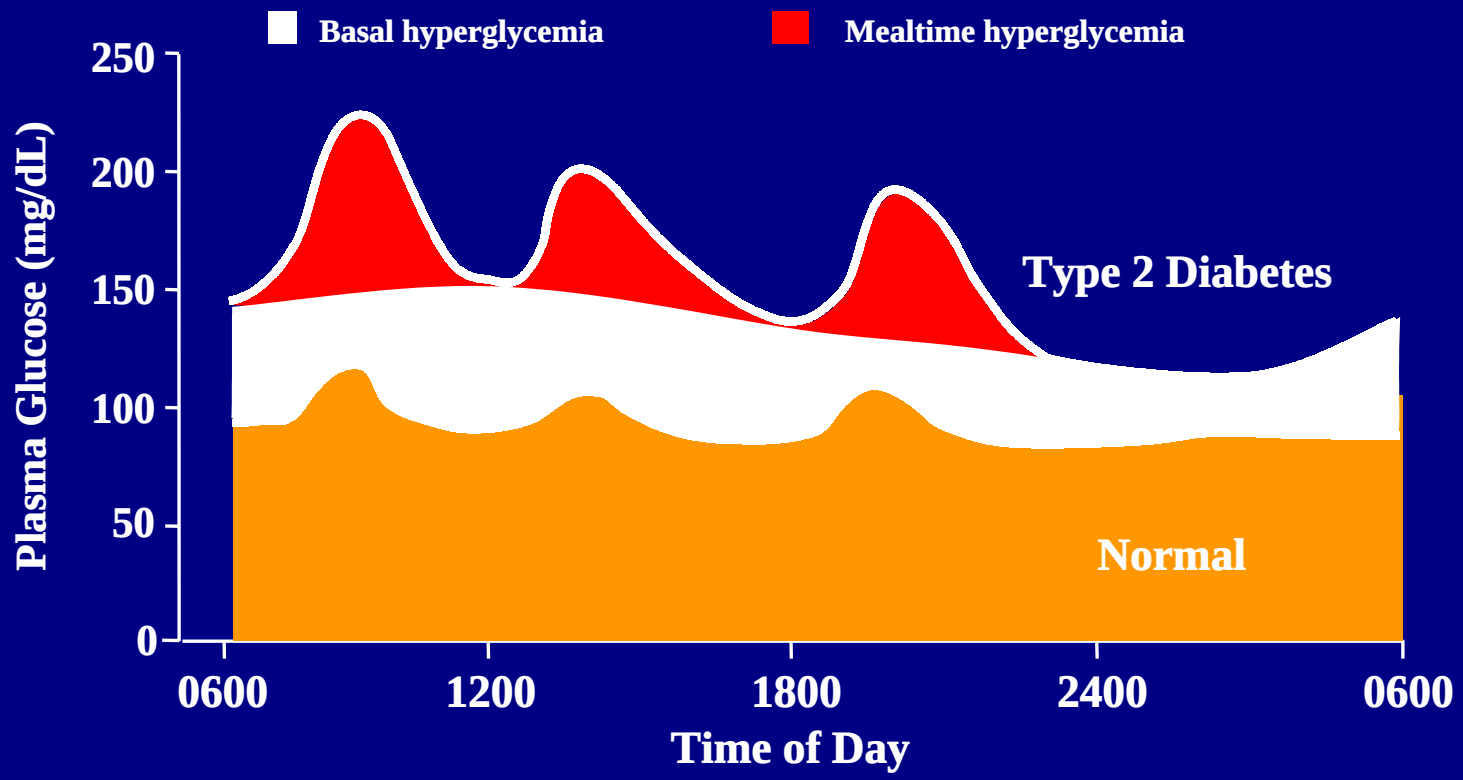
Mimicking Nature

The Basal/Bolus Insulin Concept

The Basal/Bolus Insulin Concept

- Basal insulin
  - Suppresses glucose production between meals and overnight
  - 40% to 50% of daily needs
- Bolus insulin (mealtime)
  - Limits hyperglycemia after meals
  - Immediate rise and sharp peak at 1 hour
  - 10% to 20% of total daily insulin requirement at each meal

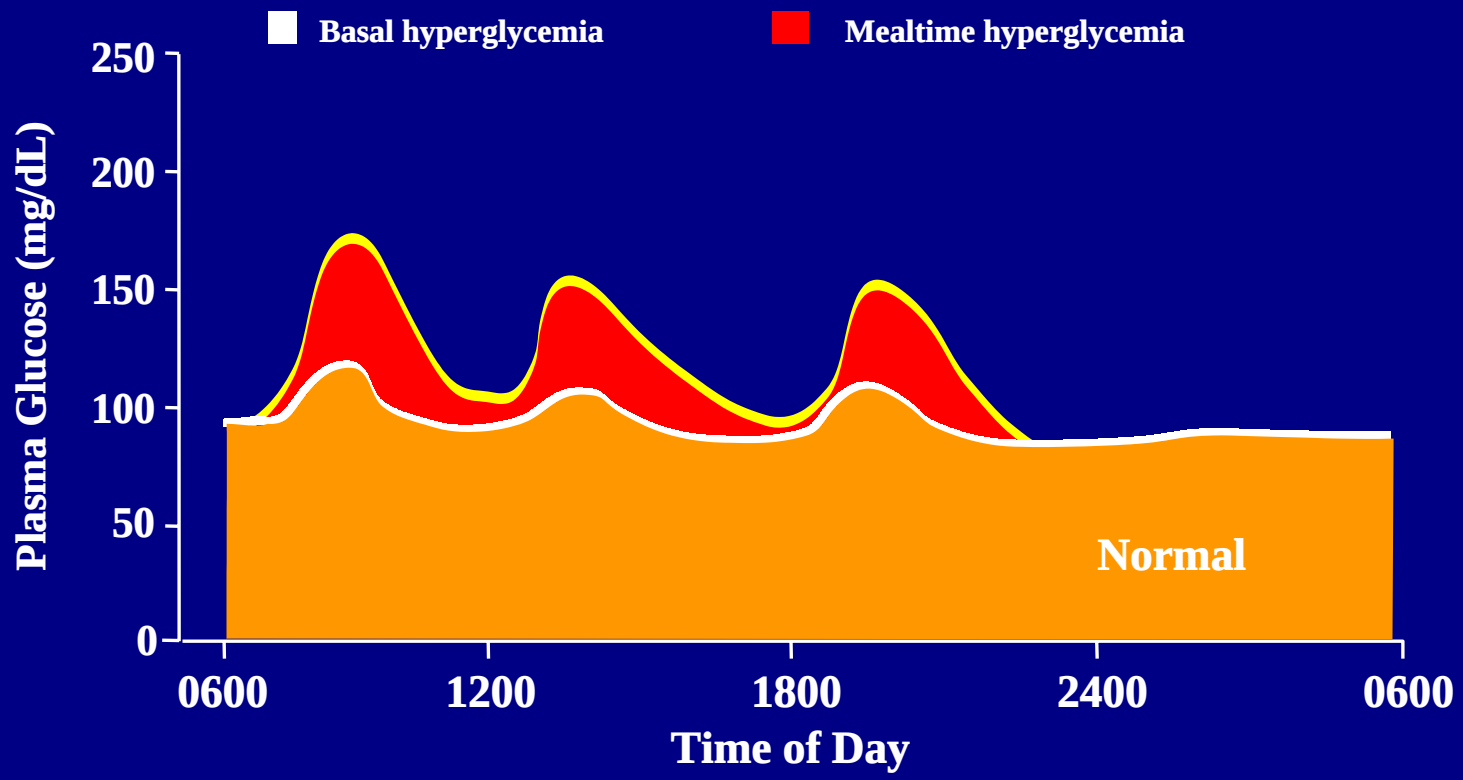
Basal vs Mealtime Hyperglycemia in Diabetes



Δ AUC from normal basal >1875 mgm/dL·hr; Est $HbA1_c$ >8.7%

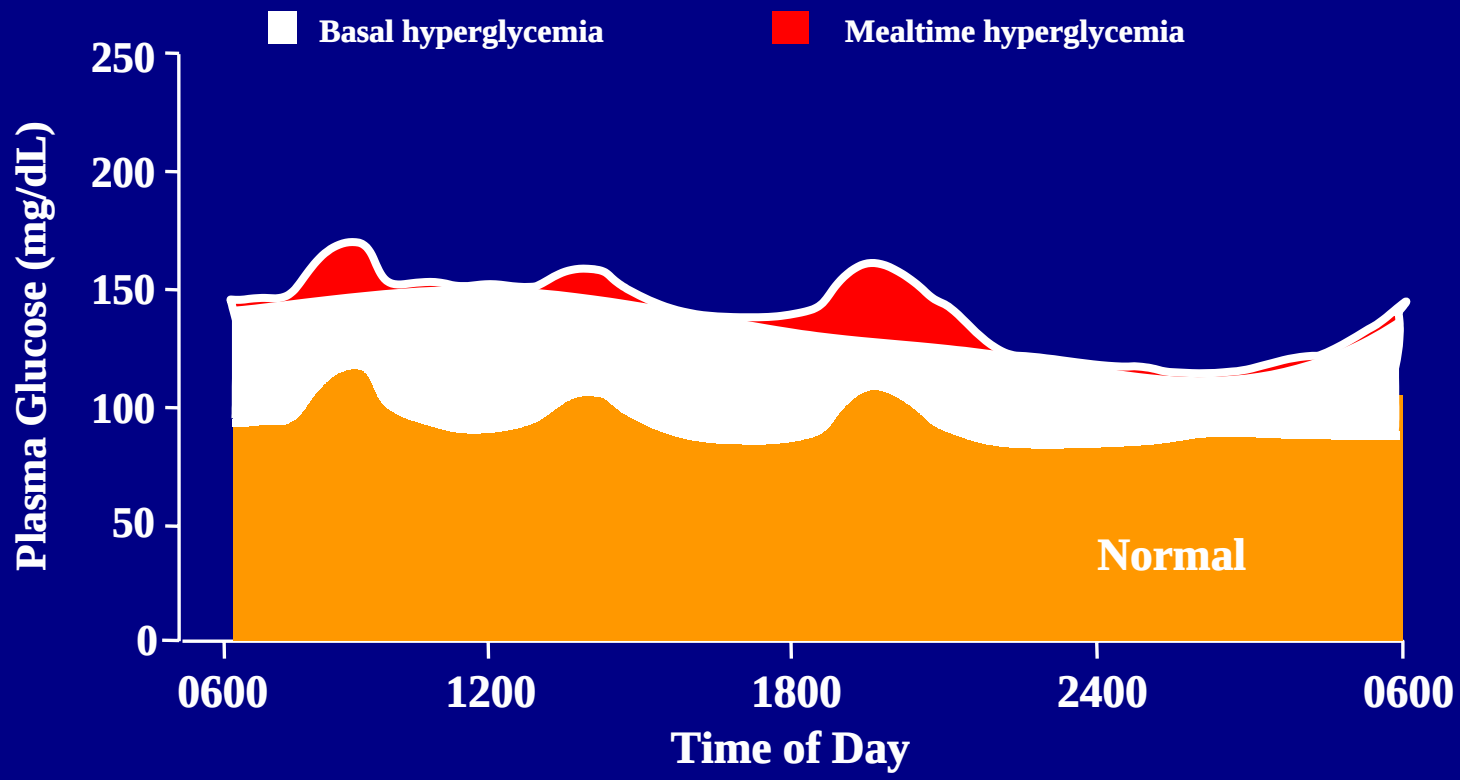
Riddle. *Diabetes Care.* 1990;13:676-686.

When Basal Corrected



Δ AUC from normal basal 900 mgm/dL·hr; Est $HbA1_c$ 7.2%

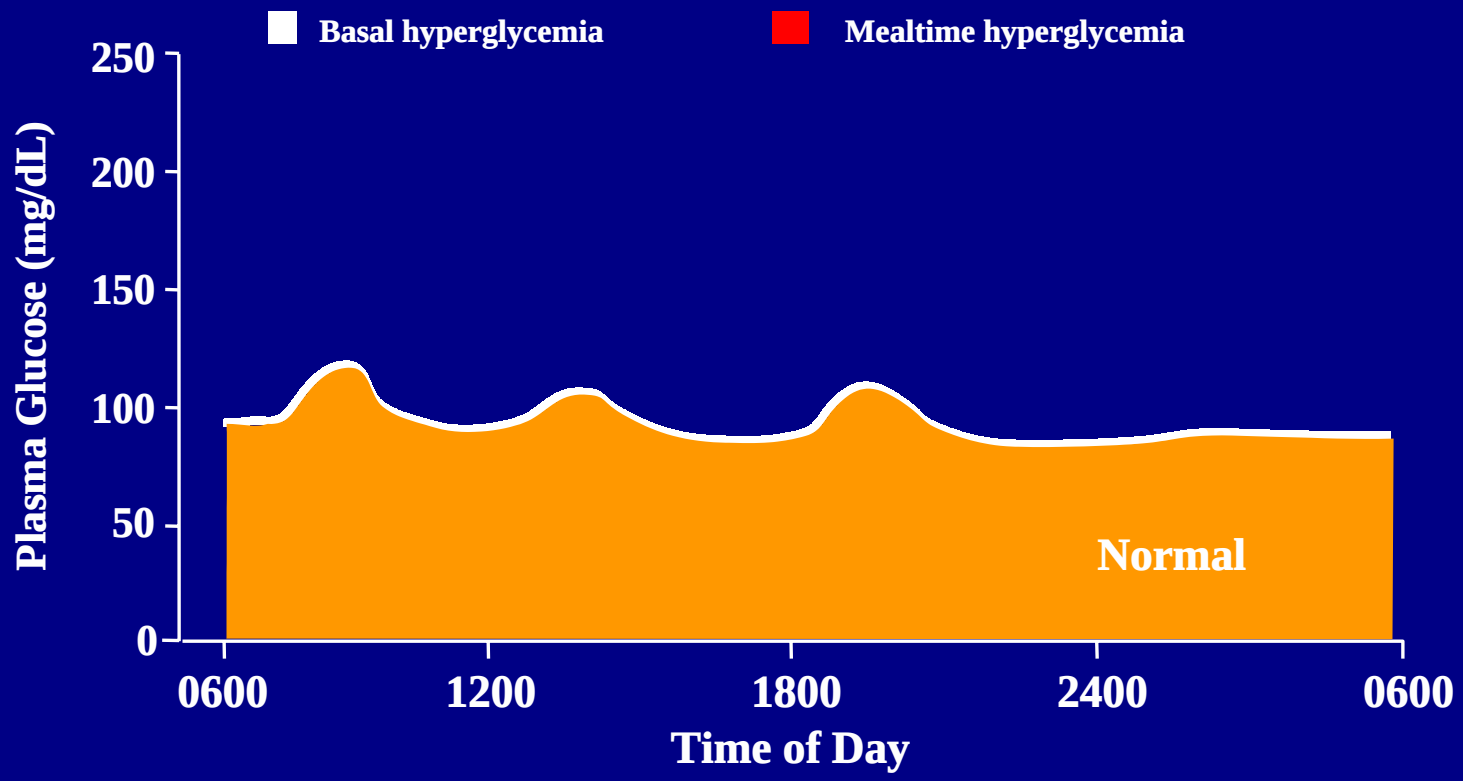
When Mealtime Hyperglycemia Corrected



Δ AUC from normal basal 1425 mgm/dL·hr; Est $HbA1_c$ 7.9

Basal vs Mealtime Hyperglycemia in Diabetes

When Both Basal & Mealtime Hyperglycemia Corrected



Δ AUC from normal basal 225 mgm/dL·hr; Est $HbA1_c$ 6.4%

MIMICKING NATURE WITH INSULIN THERAPY

Over time,

most patients will need

both basal and mealtime insulin

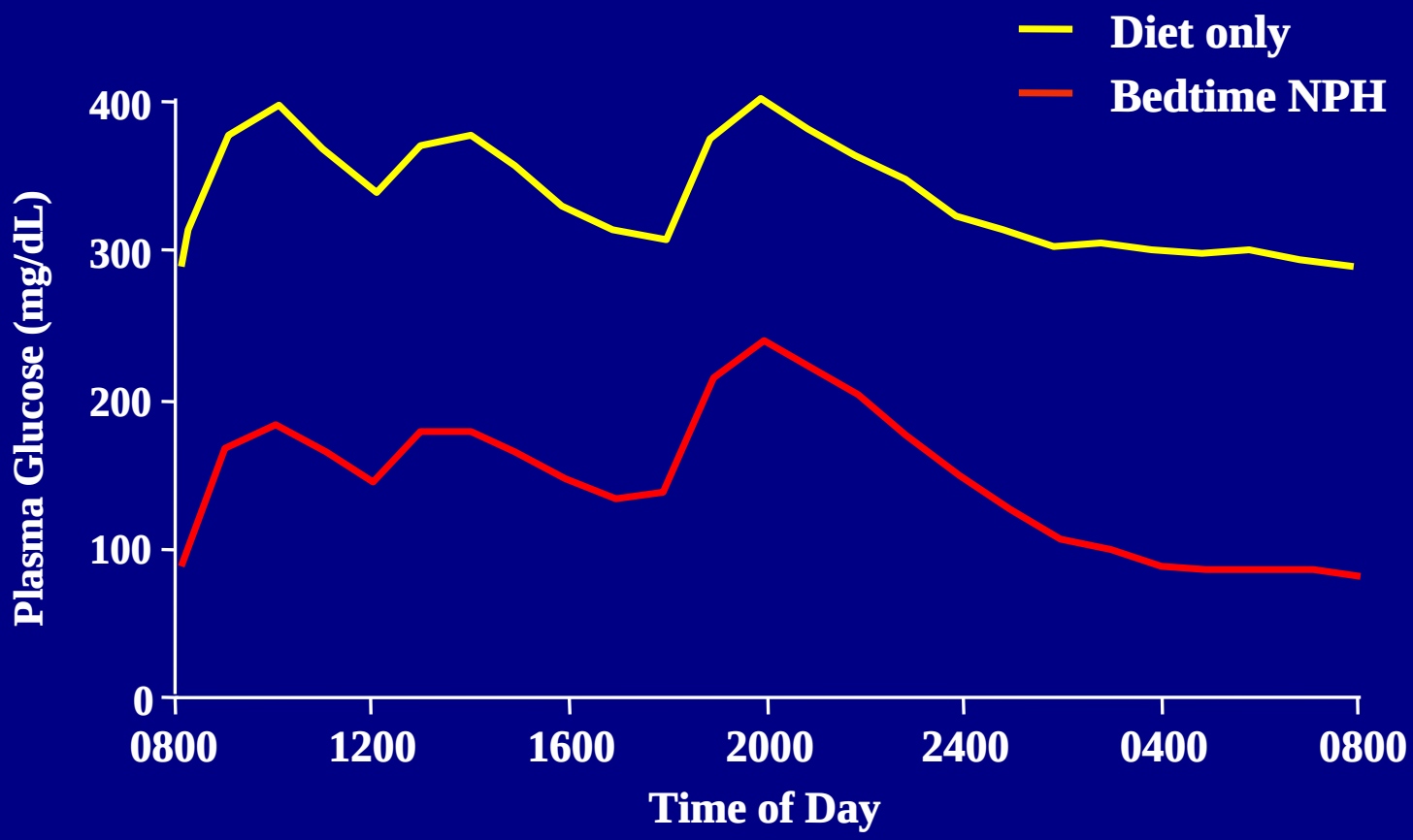
to control glucose

Starting With Basal Insulin
Advantages

- 1 injection with no mixing
- Insulin pens for increased acceptance
- Slow, safe, and simple titration
- Low dosage
- Effective improvement in glycemic control
- Limited weight gain

Starting With Basal Insulin

Bedtime NPH Added to Diet



Cusi & Cunningham. *Diabetes Care*. 1995;18:843-851.

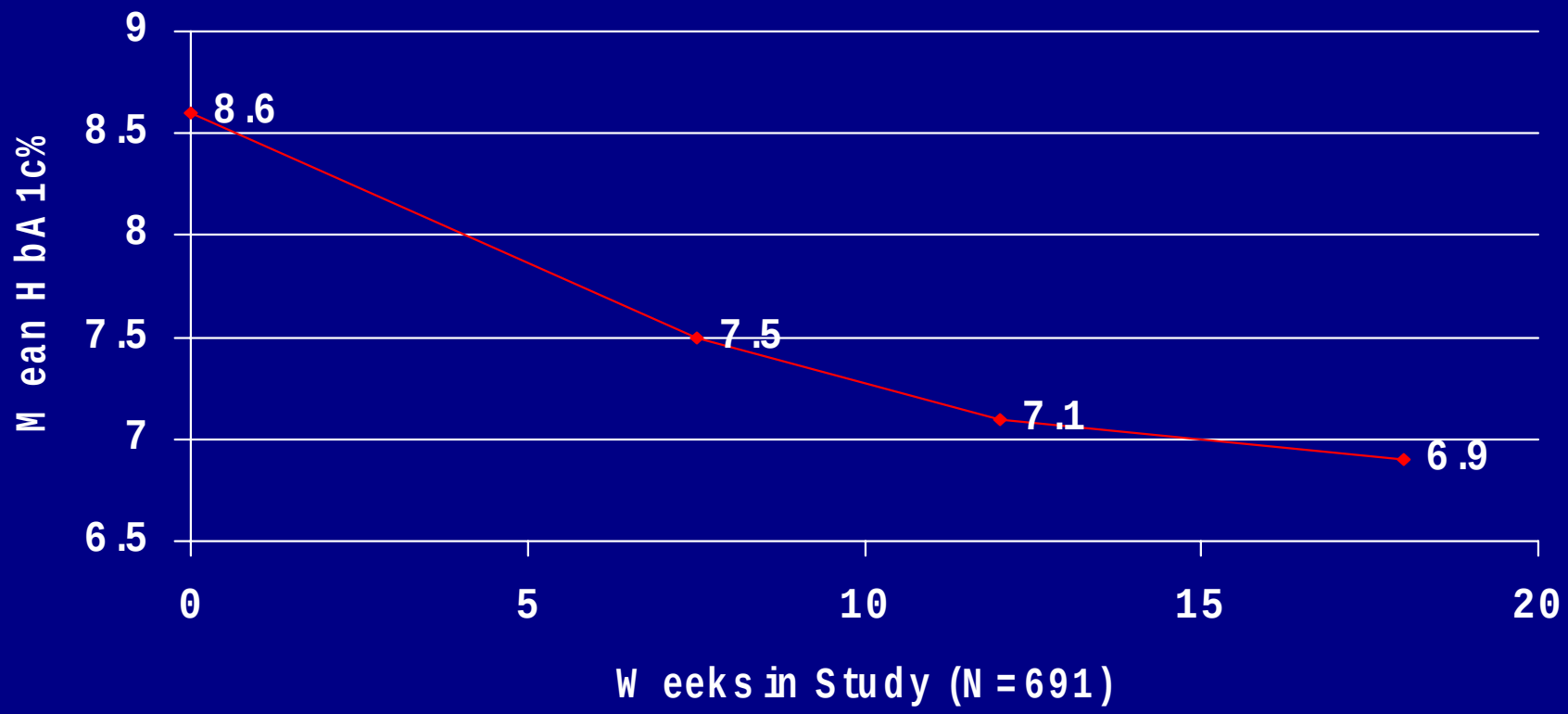
Treatment to Target Study: NPH vs Glargine in DM2 patients on OHA

- Type 2 DM on 1 or 2 oral agents (SU, MET, TZD)
- Age 30 to 70
- BMI 26 to 40
- A1C 7.5 to 10% and FPG > 140 mg/dL
- Anti GAD negative
- Willing to enter a 24 week randomized, open labeled study

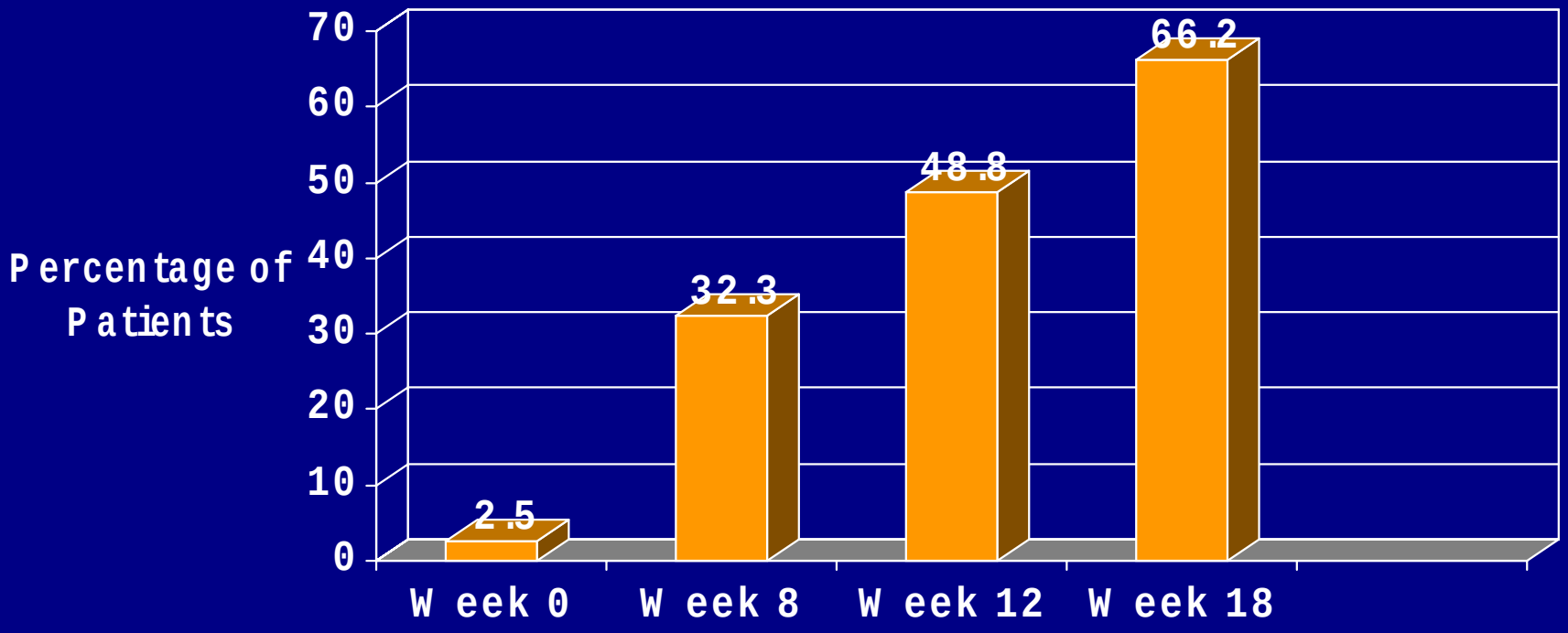
Treatment to Target Study: NPH vs Glargine in DM2 patients on OHA

- Add 10 units Basal insulin at bedtime (NPH or Glargine)
- Continue current oral agents
- Titrate insulin weekly to fasting BG < 100 mg/dL
  - if 100-120 mg/dL, increase 2 units
  - if 120-140 mg/dL, increase 4 units
  - if 140-160 mg/dL, increase 6 units
  - if 160-180 mg/dL, increase 8 units

Treatment to Target Study; A1C Decrease



Patients in Target (A1c < 7%)



Treatment to Target Study: NPH vs Glargine in DM2 patients on OHA

- Nocturnal Hypoglycemia reduced by ?% in the Glargine group

Advancing Basal/Bolus Insulin

- Indicated when FBG acceptable but
  - HbA1c > 7% or > 6.5%
    and/or
  - SMBG before dinner > 140 mg/dL
- Insulin options
  - To glargine or NPH, add mealtime aspart / lispro
  - To suppertime 70/30, add morning 70/30
  - Consider insulin pump therapy
- Oral agent options
  - Usually stop sulfonylurea
  - Continue metformin for weight control
  - Continue glitazone for glycemic stability?

Starting With Bolus Insulin

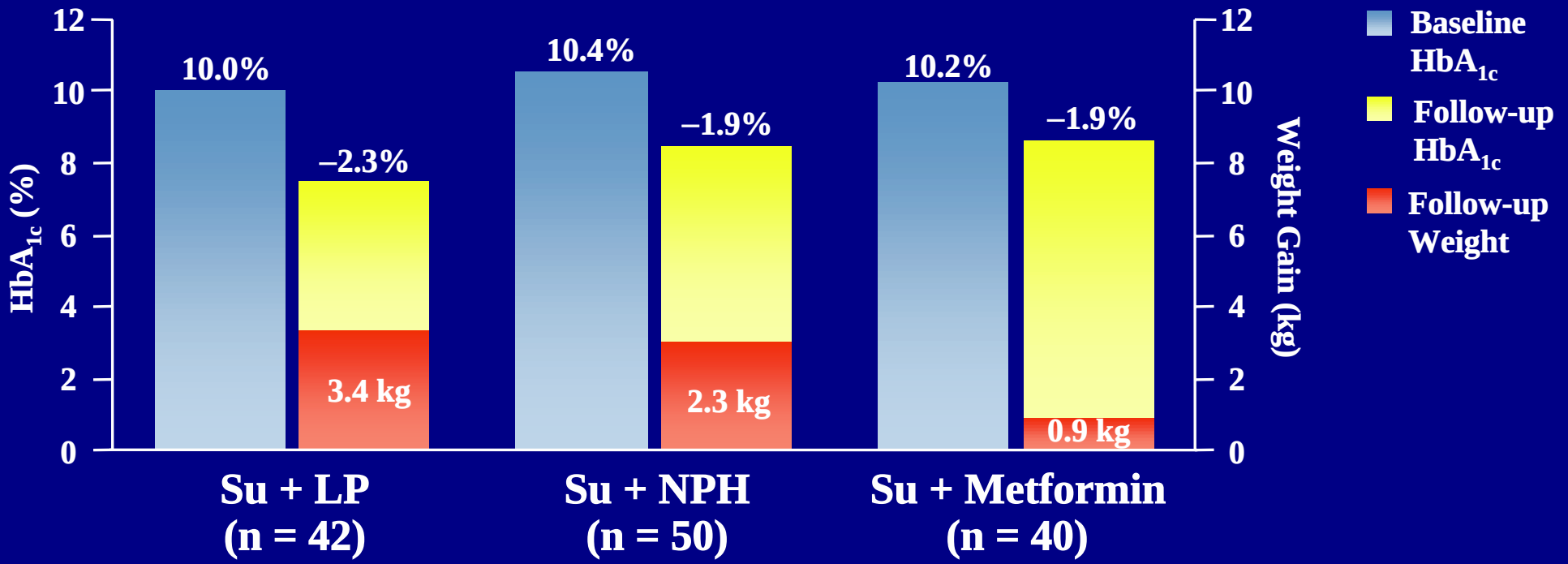
Combination Oral Agents

+

Mealtime Insulin

Starting With Bolus Insulin

Mealtime Lispro vs NPH or Metformin Added to Sulfonylurea



Browdos, et al. *Diabetes*. 1999;48(suppl 1):A104.

Case #1: DM 2 on SU with infection

- 49 year old white male
- DM 2 onset age 43, wt 173 lbs, Ht 70 inches
- On glimepiride (Amaryl) 4 mg/day , HbA1c 7.3% (intolerant to metformin)
- Infection in colostomy pouch (ulcerative colitis) glucose up to 300 mg/dL plus
- SBGM 3 times per day

Case #1: DM 2 on SU with infection

- Started on MDI; starting dose 0.2 x wgt. in lbs.
- Wgt. 180 lbs which = 36 units
- Bolus dose (lispro/aspart) = 20% of starting dose at each meal, which = 7 to 8 units ac (tid)
- Basal dose (glargine) = 40% of starting dose at HS, which = 14 units at HS
- Correction bolus = (BG - 100)/ SF, where SF = 1500/total daily dose; SF = 40

Correction Bolus Formula

$$\frac{\text{Current BG - Ideal BG}}{\text{Glucose Correction factor}}$$

Example:

- **Current BG: 220 mg/dl**
- **Ideal BG: 100 mg/dl**
- **Glucose Correction Factor: 40 mg/dl**

$$\frac{220 - 100}{40} = 3.0\text{u}$$

Case #1: DM 2 on SU with infection

- Started on MDI
- Did well, average BG 138 mg/dL at 1 month and 117 mg/dL at 2 months post episode with HbA1c 6.1%

Strategies to Improve Glycemic Control: Type 2 Diabetes

- Monitor glycemic targets – Fasting and postprandial glucose, HbA_{1c}
- Self-monitoring of blood glucose is essential
- Nutrition and activity are cornerstones of therapy
- Combinations of pharmacologic agents are often necessary to achieve glycemic targets

Intensive Therapy for Type 1 Diabetes

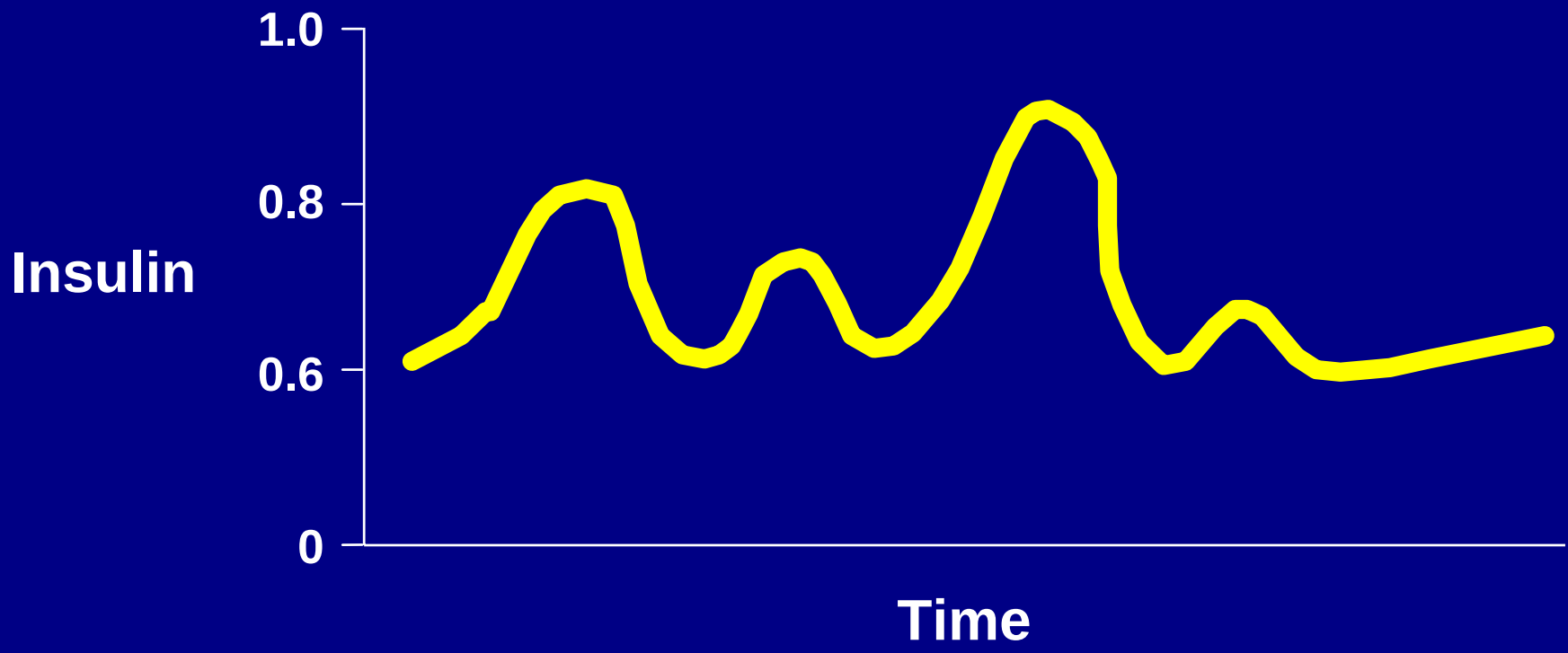
- Careful balance of food, activity, and insulin
- Daily self-monitoring BG
- Patient trained to vary insulin and food
- Define target BG levels (individualized)
- Frequent contact of patient and diabetes team
- Monitoring HbA_{1c}
- Basal / Bolus insulin regimen

Options in Insulin Therapy

- Current
  - Multiple injections
  - Insulin pump (CSII)
- Future
  - Implant (artificial pancreas)
  - Transplant (pancreas; islet cells)

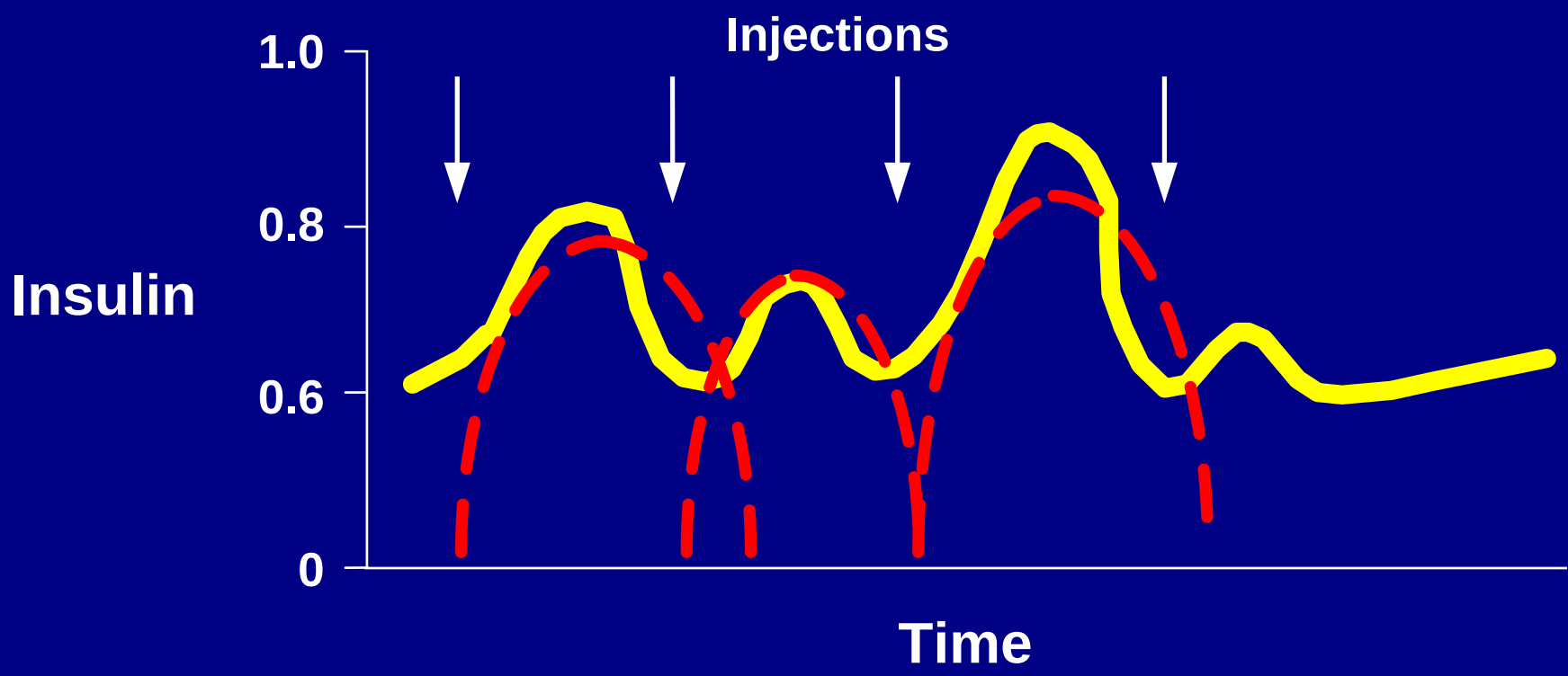
Multiple Injection Therapy

Intermediate & Short-Acting Insulin Pre-Meal



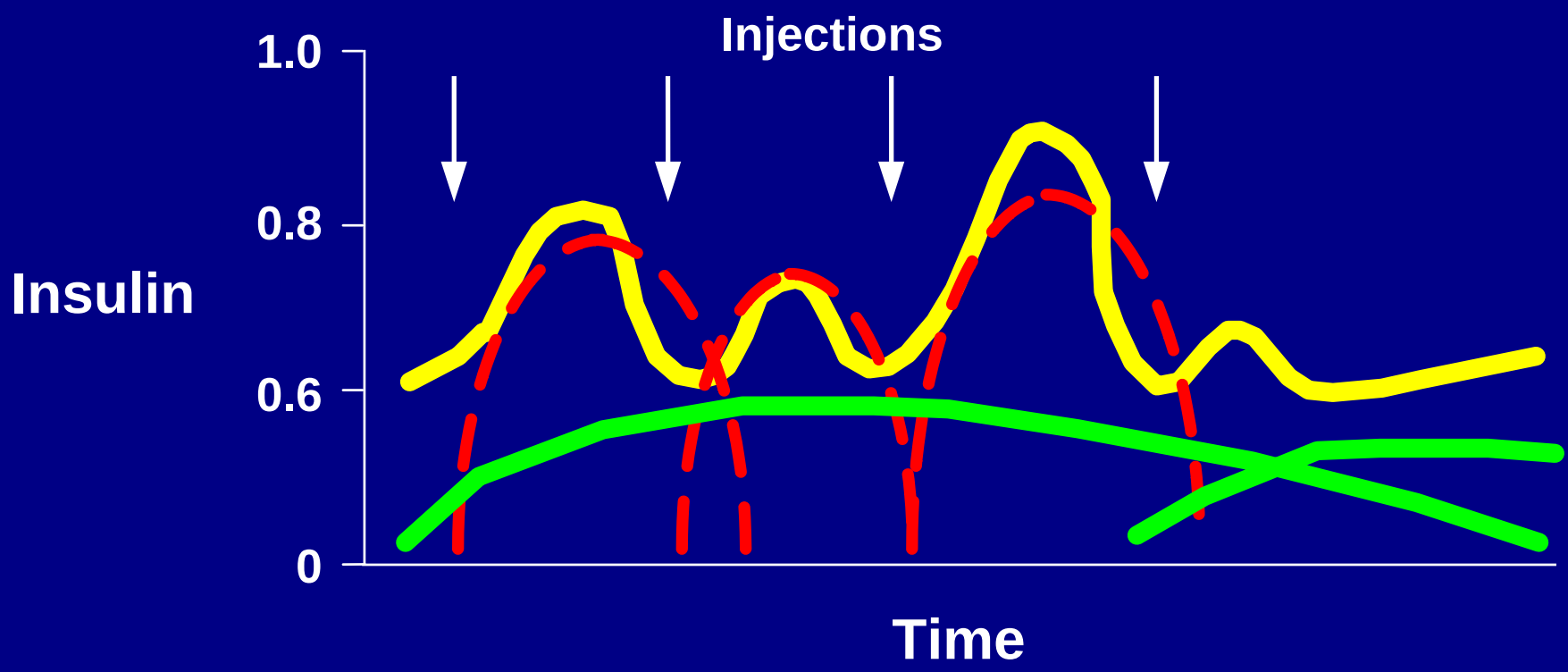
Multiple Injection Therapy

Intermediate & Short-Acting Insulin Pre-Meal



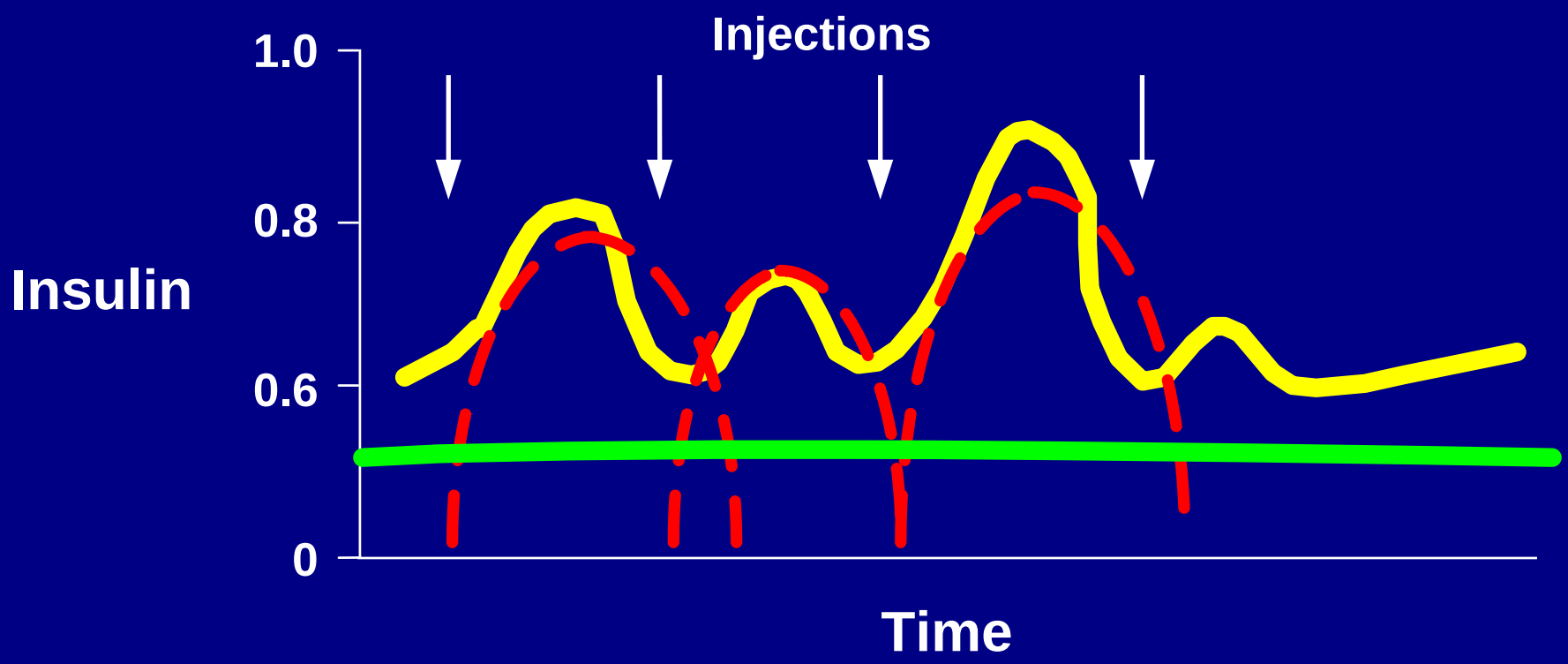
Multiple Injection Therapy

Intermediate & Short-Acting Insulin Pre-Meal



Multiple Injection Therapy

Glargine & Short-Acting Insulin Pre-Meal



Case #2: DM 1 on MDI

- 46 year old white male power line supervisor
- DM 1 age 40
- On MDI: 10 u lispro pre-meal, 20 u NPH HS
- HbA1c 7.4%
- SMBG avg 124 mg/dL based on 1.9 tests/day (fasting 171 mg/dL, noon 105 mg/dL, pm 125 mg/dL, HS 75 mg/dL)

Case #2: DM 1 on MDI

- Lantus (glargine) 20 u HS added in place of NPH
- No change in behavior (diet, SMBG frequency)
- Seen three months later (8-16-01)
- HbA1c 6.3%
- SMBG average 104 mg/dL (fasting BG 91 mg/dL, noon 126 mg/dL, pm 116 mg/dL, HS 126 mg/dL
- NO HYPOGLYCEMIA
- HAPPY

Insulin Pens

Introducing InDuo™

- The world's first combined insulin doser and blood glucose monitoring system
- A major break-through in Diabetes Care

InDuo™ - Integration

Feature

- Combined insulin doser and blood glucose monitor

InDuo™ - Compact Size

Feature

- Compact, discreet design

Benefit

- Allows discreet testing and injecting anywhere, anytime

InDuo™ - Doser Remembers

Feature

- Remembers amount of insulin delivered and time since last dose

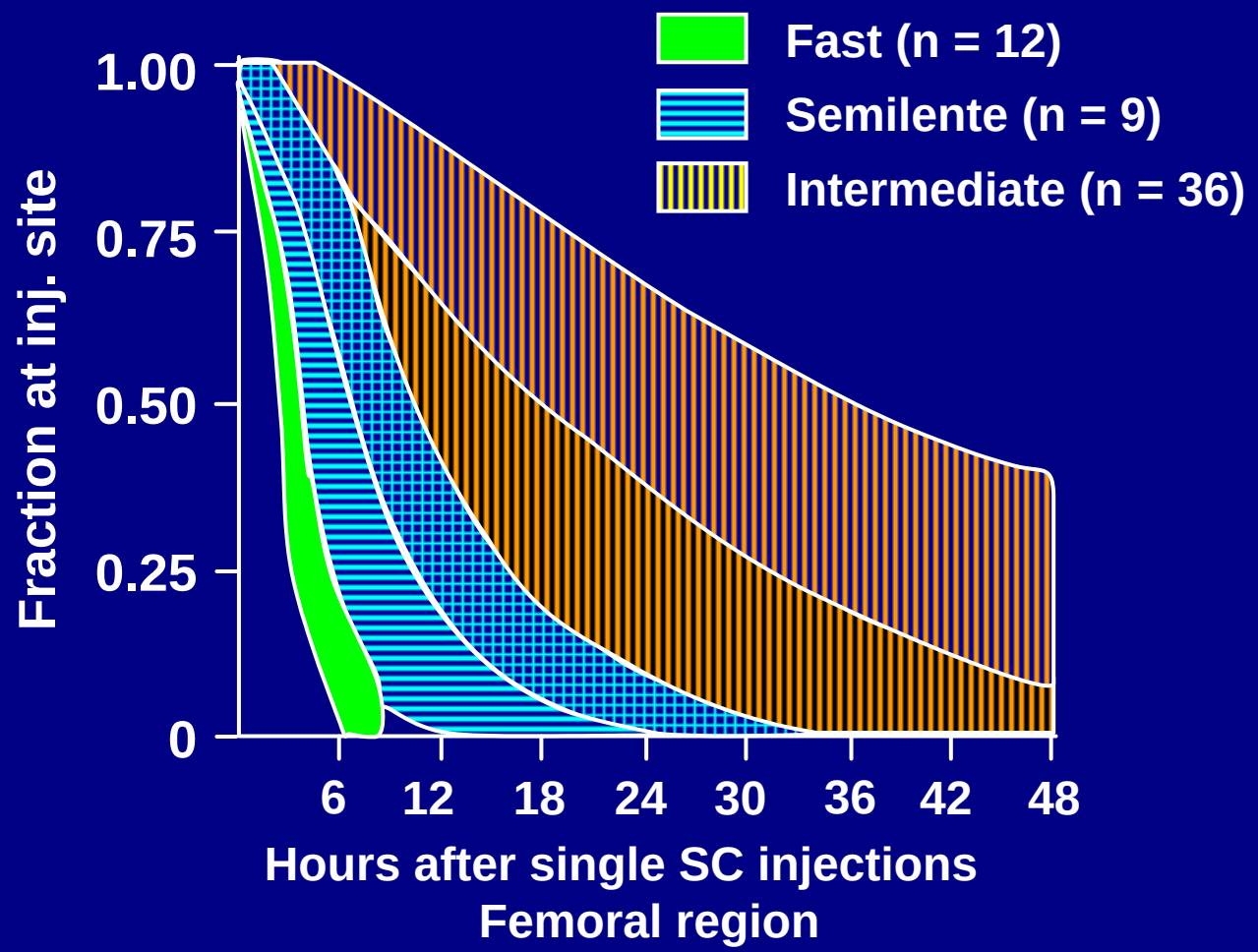
Benefit

- Helps people inject the right amount of insulin at the right time

Variability of Insulin Absorption

CSII <2.8%

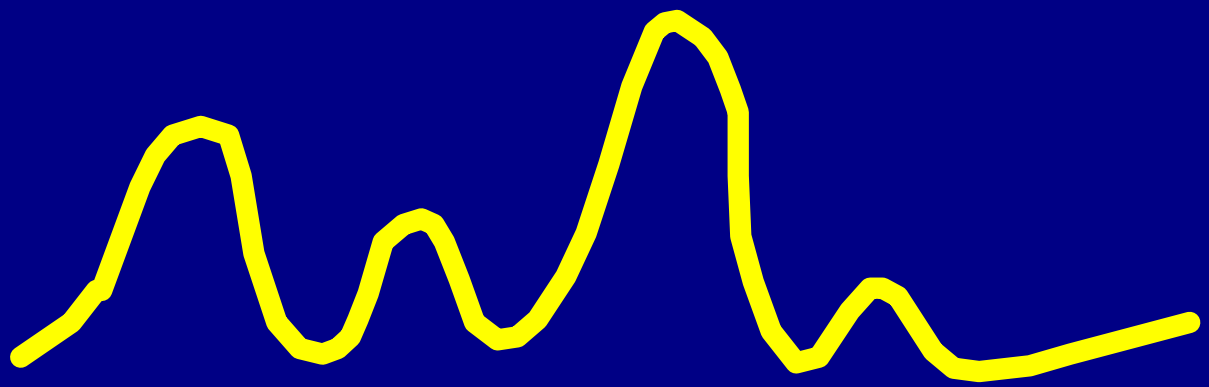
Subcutaneous Injectable 10% to 52%



Lauritzen. *Diabetologia.* 1983;24:326–329.

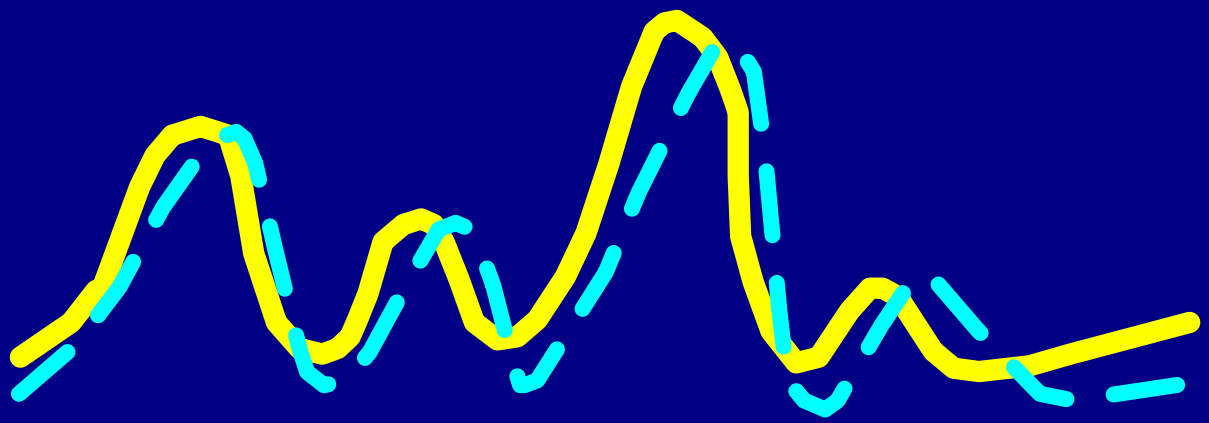
Pump Therapy

Basal & Bolus Short-Acting Insulin



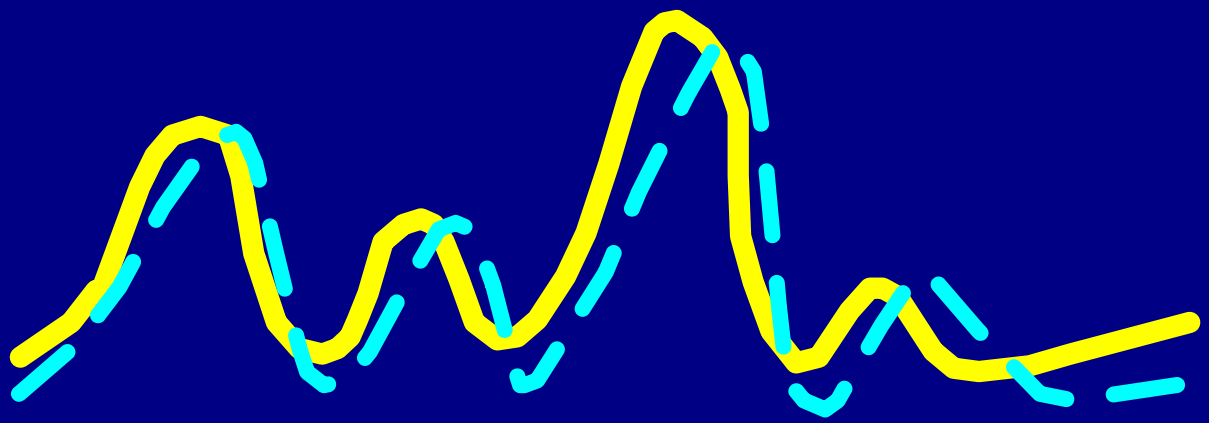
Pump Therapy

Basal & Bolus Short-Acting Insulin



Pump Therapy

Basal & Bolus Short-Acting Insulin

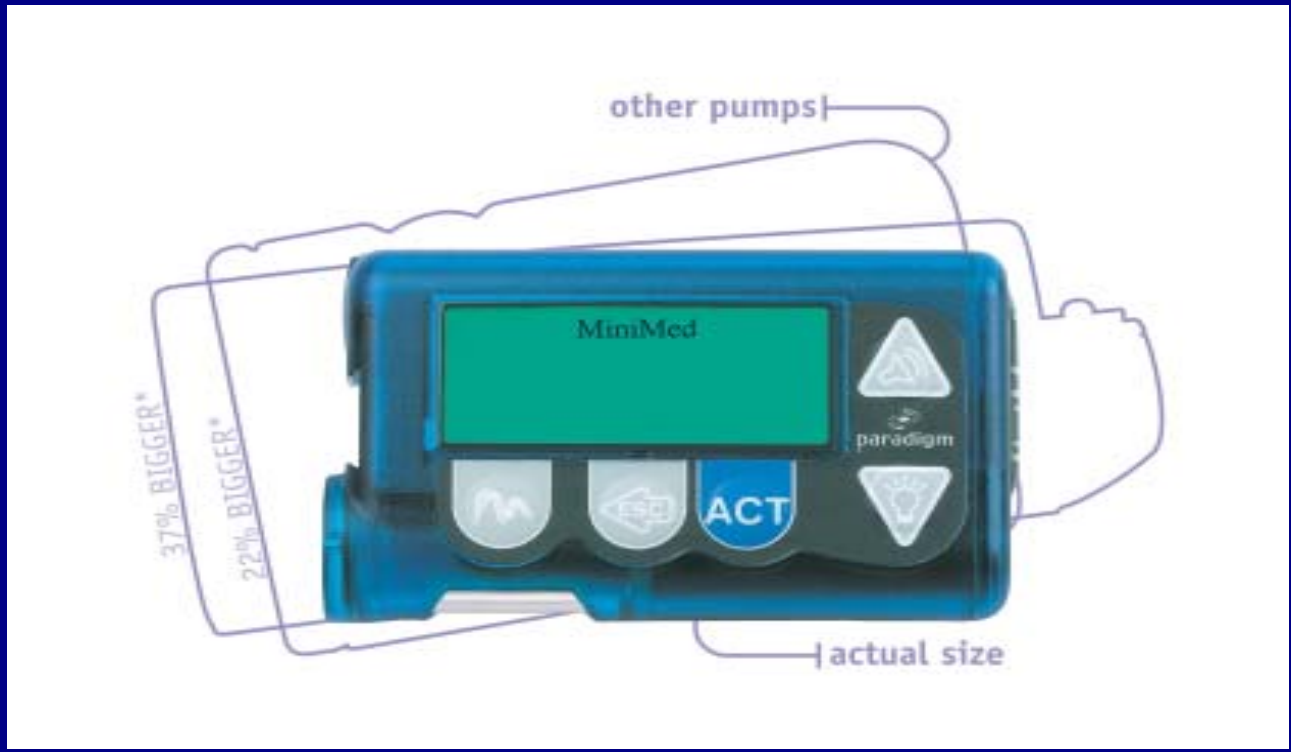


- Combined with SMBG, physiologic insulin requirements can be achieved more closely
- Flexibility in lifestyle

History of Pumps


MiniMed 508
12:43 PM
sel
act
stop
bol
act
MiniMed

PARADIGM PUMP



Paradigm.
Simple. Easy.

Paradigm Pump: Advantages

- 29% smaller, water resistant
- Menu driven:

  bolus, suspend, basal, prime, utilities
- Reservoir based (easier to fill)
- Silent motor
- AAA batteries

Paradigm Pump: Advantages

- Various bolus options

  normal, square, dual, and “easy bolus”

- Enhanced memory
- Enhanced safety features

  (low reservoir alarm, auto off, etc.)

Pump Infusion Sets

Softset QR

Silhouette

Pharmacokinetic Advantages
CSII vs MDI

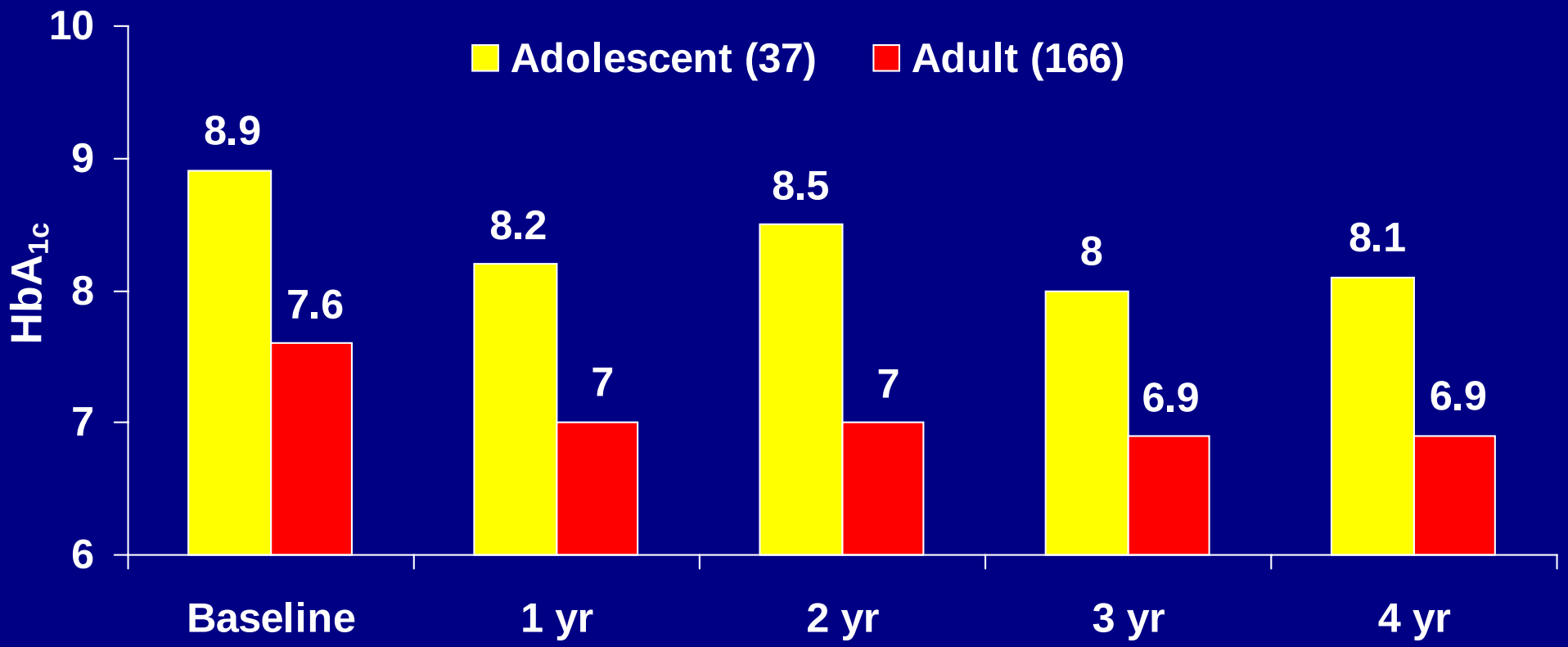
- Uses only regular or very rapid insulin
  - More predictable absorption than modified insulins (variation 3% vs 19 to 52%)
- Uses 1 injection site
  - Reduces variations in absorption due to site rotation
- Eliminates most of the subcutaneous insulin depot
- Programmable delivery simulates normal pancreatic function

Lauritzen. *Diabetologia*. 1983;24:326–329.

Metabolic Advantages with CSII

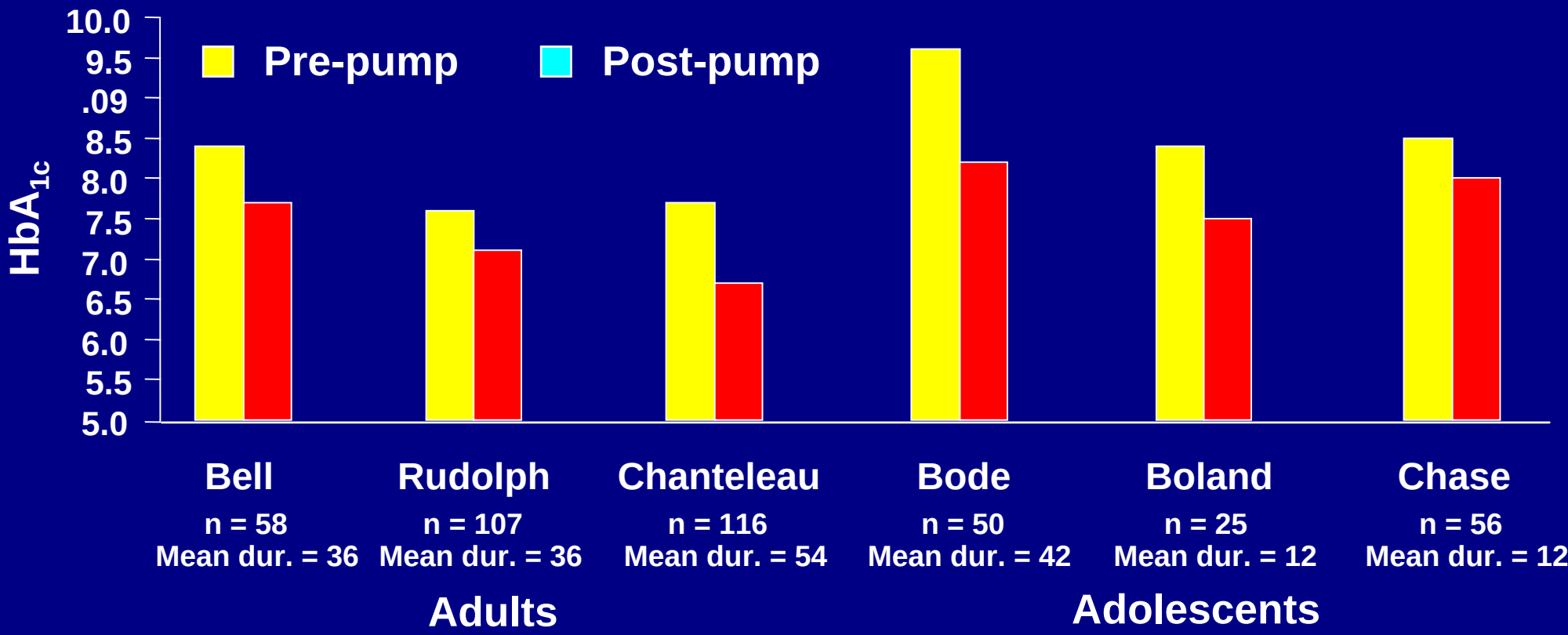
- Improved glycemic control
- Better pharmacokinetic delivery of insulin
  - Less hypoglycemia
  - Less insulin required
- Improved quality of life

Glycemic Control



Atlanta Diabetes Associates

CSII Reduces HbA_{1c}



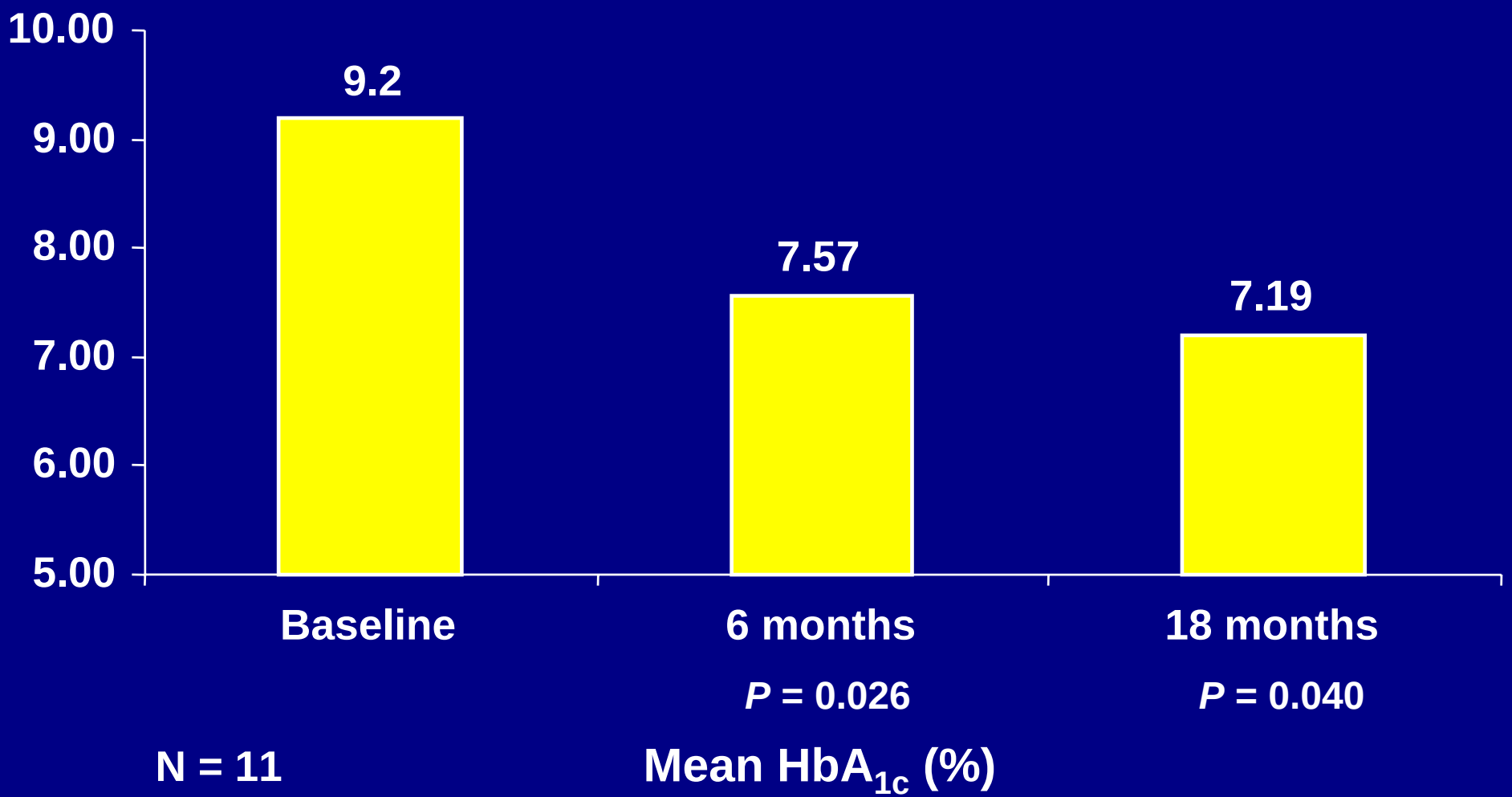
Chantelau E, et al. *Diabetologia*. 1989;32:421–426; Bode BW, et al. *Diabetes Care*. 1996;19:324–327; Boland EA, et al. *Diabetes Care*. 1999;22:1779–1784; Bell DSH, et al. *Endocrine Practice*. 2000;6:357–360; Chase HP, et al. *Pediatrics*. 2001;107:351–356.

CSII
Factors Affecting HbA_{1c}

- Monitoring
  - HbA_{1c} = 8.3 - (0.21 x BG per day)
- Recording 7.4 vs 7.8
- Diet practiced
  - CHO: 7.2
  - Fixed: 7.5
  - Other: 8.0
- Insulin type
  - Lispro: 7.3
  - R: 7.7

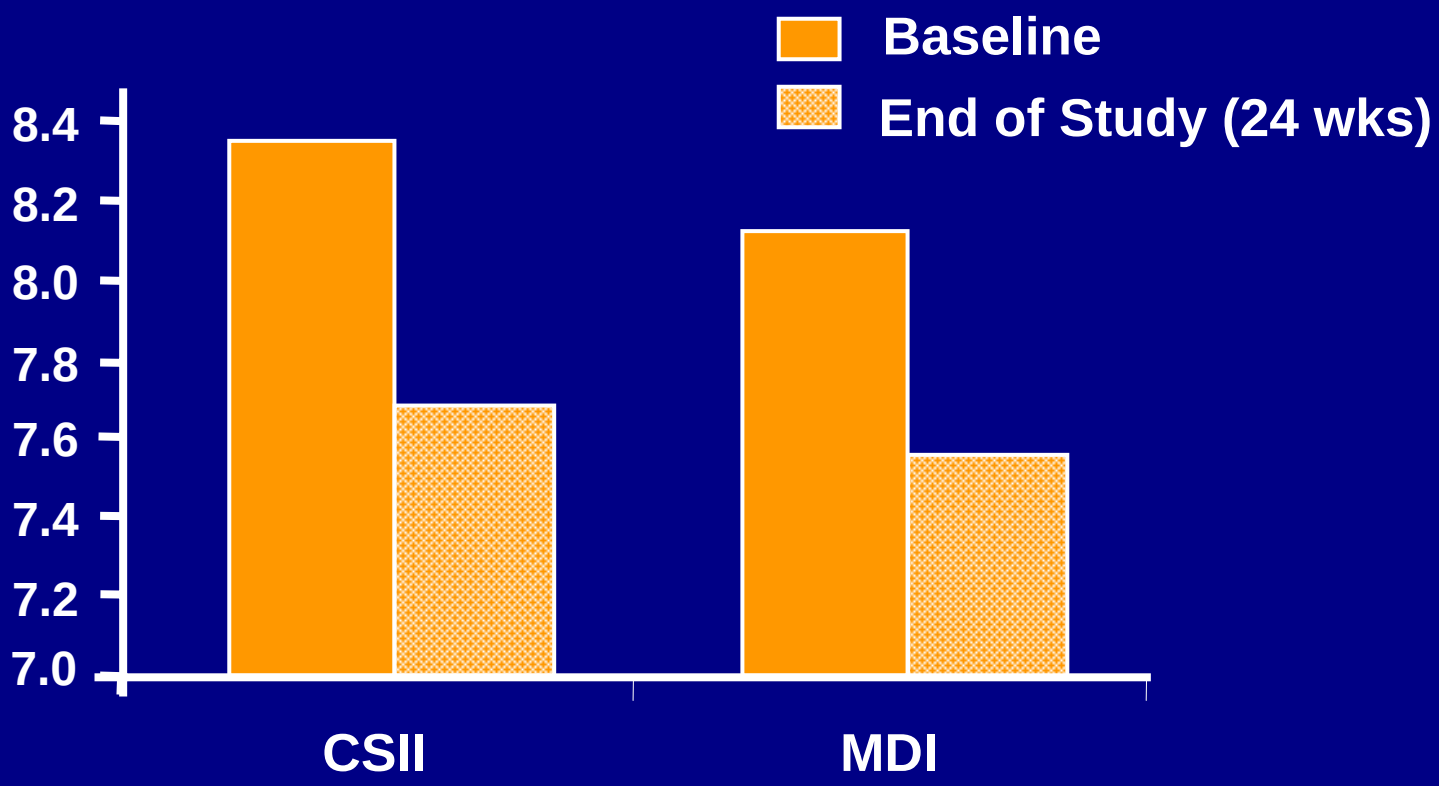
CSII Usage in Type 2 Patients

Atlanta Diabetes Experience



Glycemic Control in Type 2 DM: CSII *vs* MDI in 127 patients

- A1C

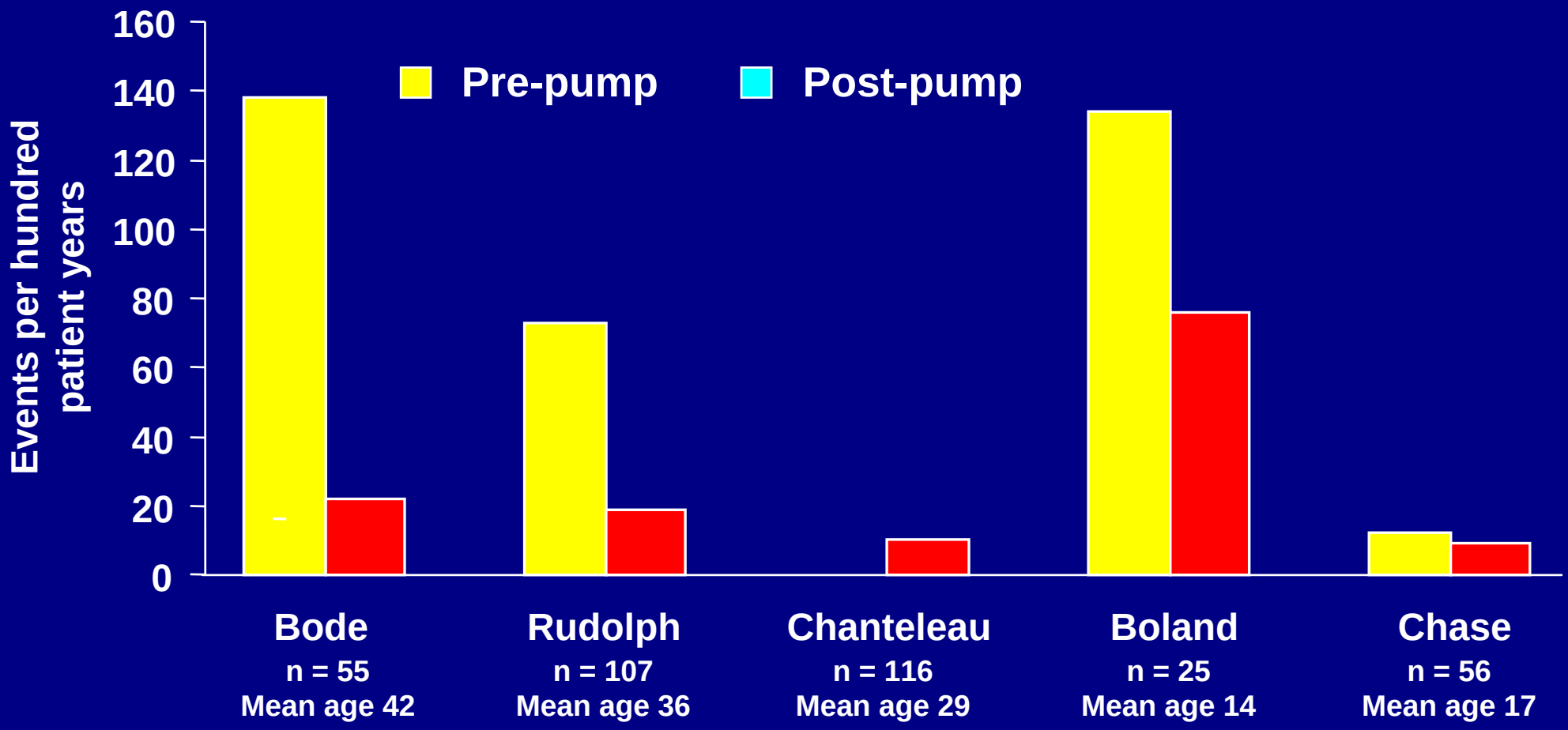


Raskin, *Diabetes* 2001; 50(S2):A106

DM 2 Study: CSII vs MDI

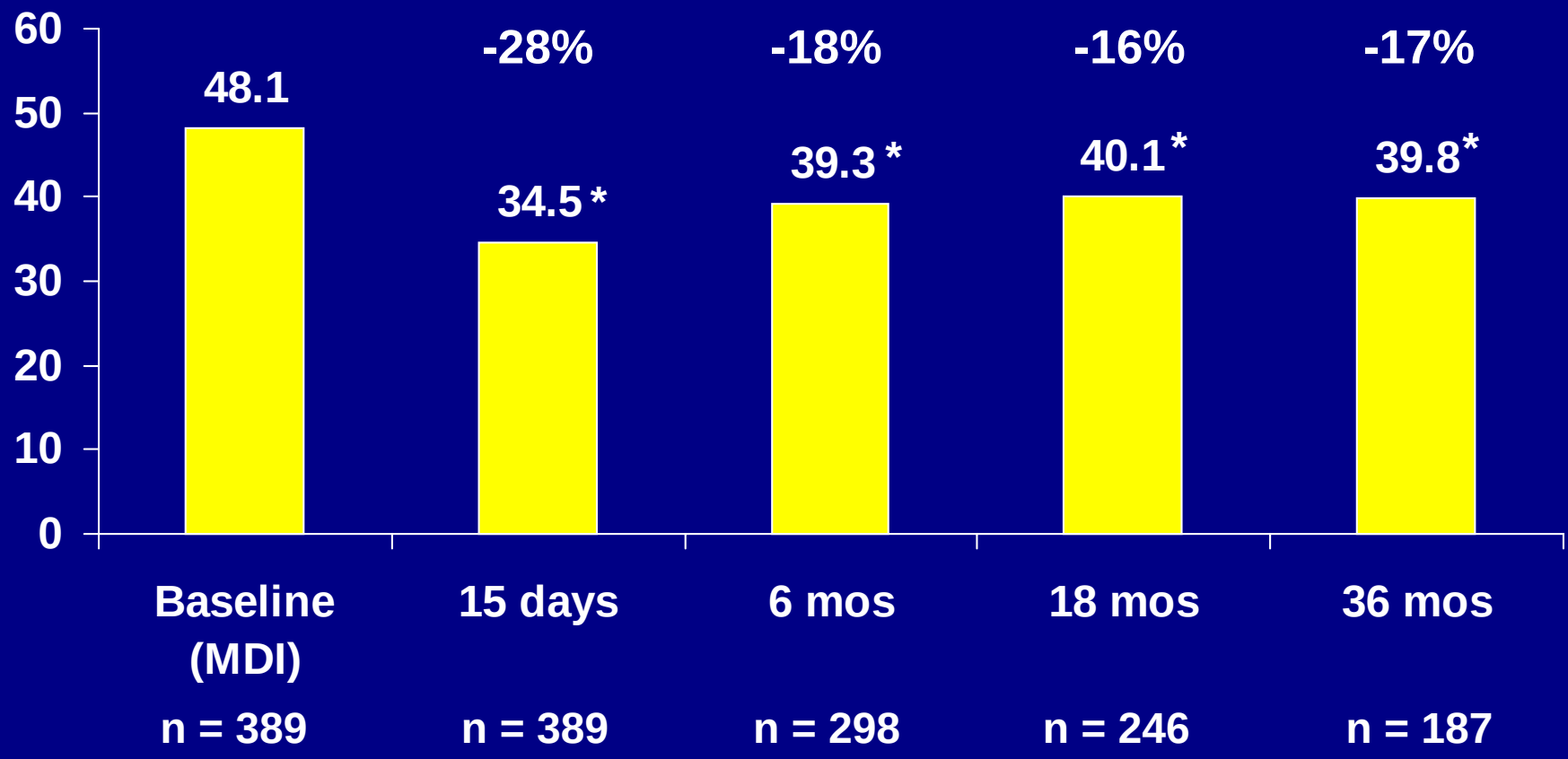
- Overall treatment satisfaction improved in the CSII group: 59% pre to 79% at 24 weeks
- 93% in the CSII group preferred the pump to their prior regiment (insulin +/- OHA)
- CSII group had less hyperglycemic episodes (3 subjects, 6 episodes vs. 11 subjects, 26 episodes in the MDI group)

CSII Reduces Hypoglycemia



Chantelau E, et al. *Diabetologia*. 1989;32:421–426; Bode BW, et al. *Diabetes Care*. 1996;19:324–327; Boland EA, et al. *Diabetes Care*. 1999;22:1779–1784; Chase HP, et al. *Pediatrics*. 2001;107:351–356.

Insulin Reduction Following CSII



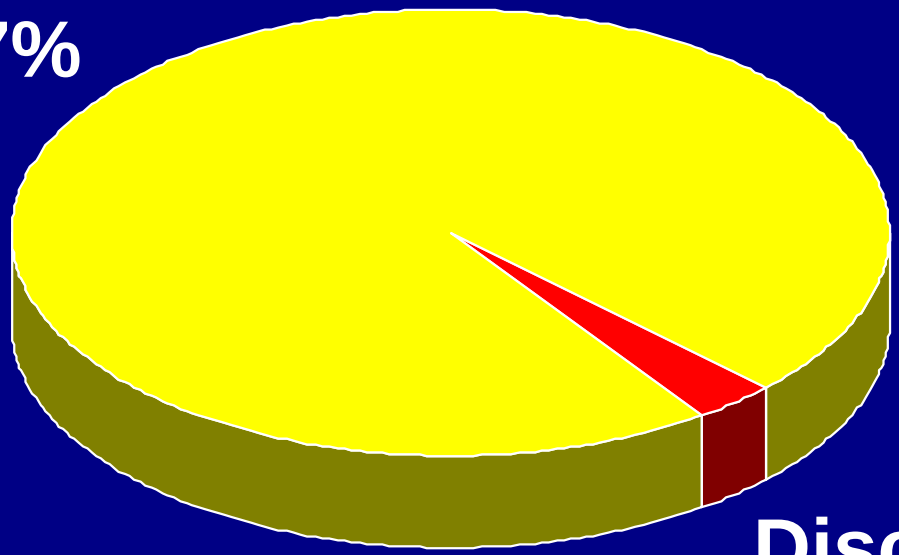
* *P* <0.001

Normalization of Lifestyle

- Liberalization of diet — timing & amount
- Increased control with exercise
- Able to work shifts & through lunch
- Less hassle with travel — time zones
- Weight control
- Less anxiety in trying to keep on schedule

Current Continuation Rate

Continuous Subcutaneous Insulin Infusion (CSII)

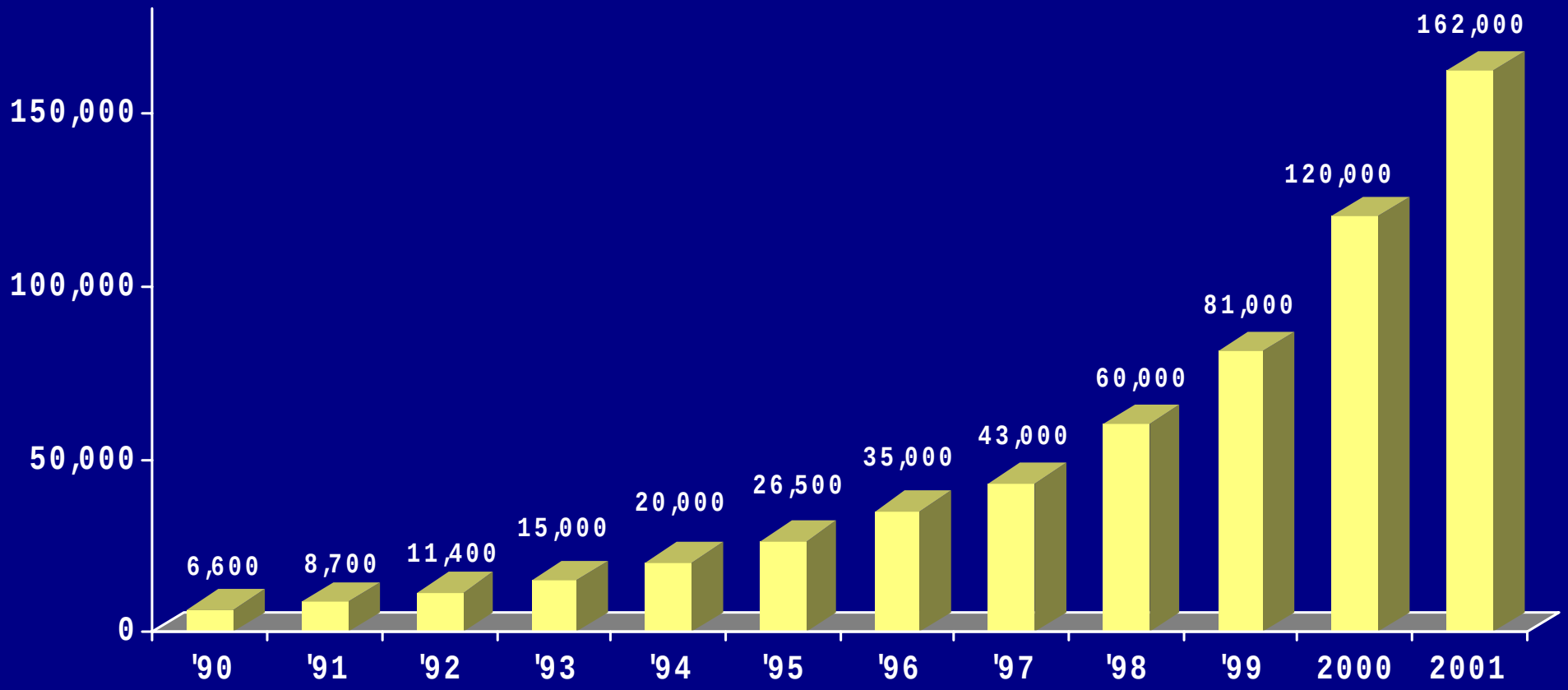


N = 165
Average Duration = 3.6 years
Average Discontinuation <1%/yr

Bode BW, et al. *Diabetes*. 1998;47(suppl 1):392.

U.S. Pump Usage

Total Patients Using Insulin Pumps



Pump Therapy Indications

- HbA_{1c} >7.0%
- Frequent hypoglycemia
- Dawn phenomenon
- Exercise
- Pediatrics
- Pregnancy
- Gastroparesis
- Hectic lifestyle
- Shift work
- Type 2

Marcus. *Postgrad Med*. 1995.

Poor Candidates for CSII

- Unwilling to comply with medical follow-up
- Unwilling to perform self blood glucose monitoring 4 times daily
- Unwilling to quantitate food intake

Current Candidate Selection

Patient Requirements

- Willing to monitor and record BG
- Motivated to take insulin
- Willing to quantify food intake
- Willing to follow-up
- Interested in extending life

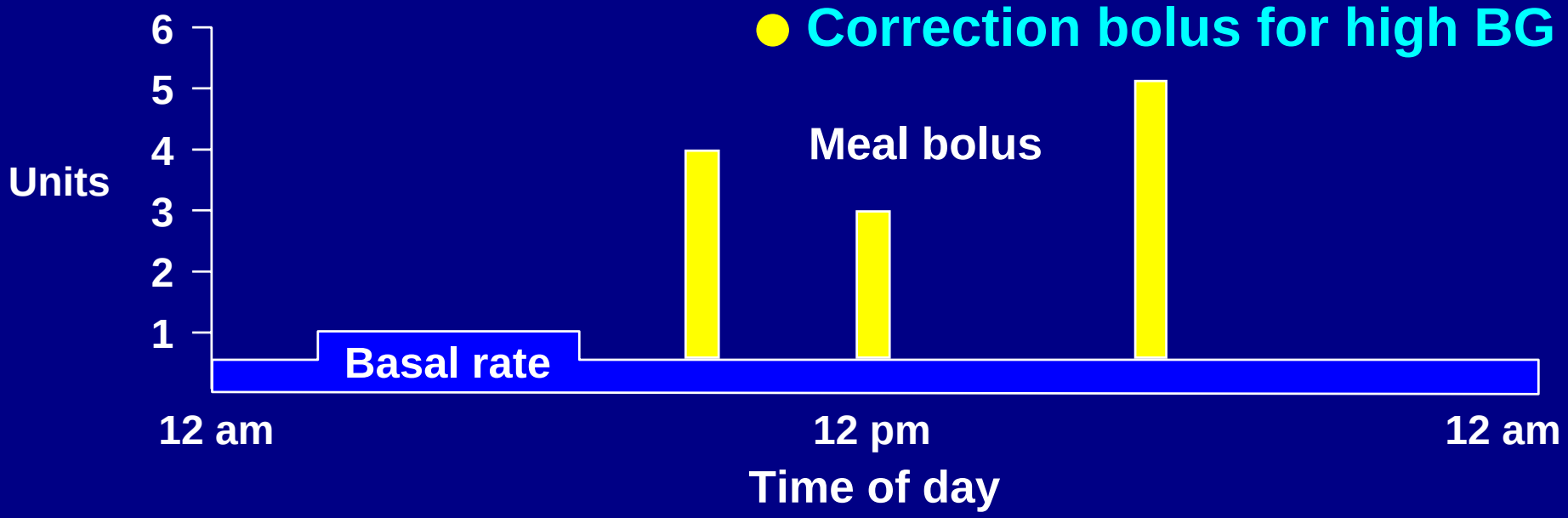
Pump Therapy

Basal rate

- Continuous flow of insulin
- Takes the place of NPH or glargine insulin

Meal boluses

- Insulin needed pre-meal
  - Pre-meal BG
  - Carbohydrates in meal
  - Activity level
- Correction bolus for high BG



What Type of Bolus Should You Give?

- 9 DM 1 patients on CSII ate pizza and coke on four consecutive Saturdays
- Dual wave bolus (70% at meal, 30% as 2-h square):

  9 mg/dl glucose rise
- Single bolus: 33 mg/dl rise
- Double bolus at -10 and 90 min: 66 mg/dl rise
- Square wave bolus over 2 hours: 80 mg/dl rise

Chase et al, Diabetes June 2001 #365

If HbA_{1c} is Not to Goal

Must look at:

- SMBG frequency and recording
- Diet practiced
  - Do they know what they are eating?
  - Do they bolus for all food and snacks?
- Infusion site areas
  - Are they in areas of lipohypertrophy?
- Other factors:
  - Fear of low BG
  - Overtreatment of low BG

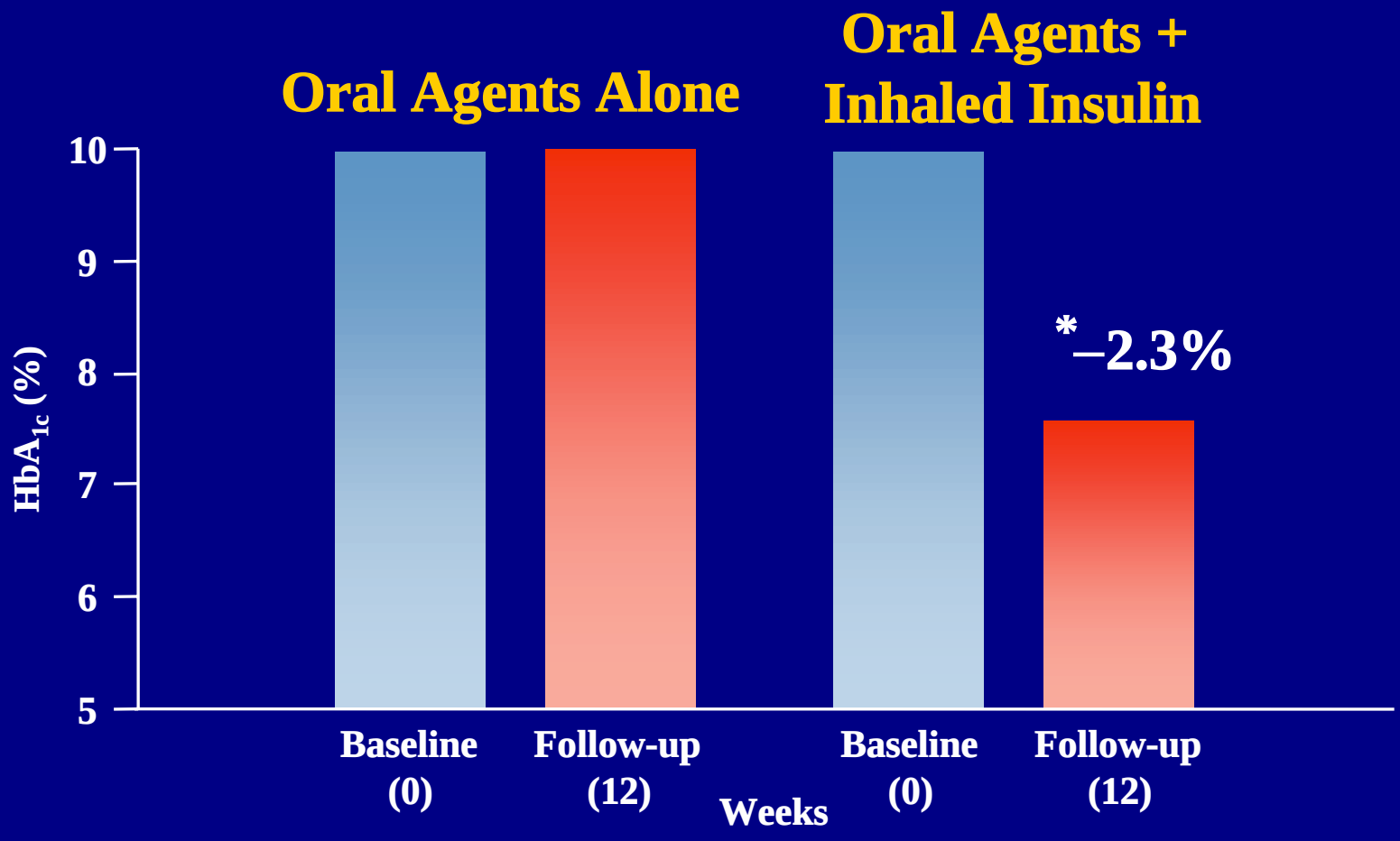
Future of Diabetes Management

Improvements in Insulin & Delivery

- Insulin analogs and inhaled insulin
- External pumps
- Internal pumps
- Continuous glucose sensors
- Closed-loop systems

Pulmonary Insulin

Oral Agents + Mealtime Inhaled Insulin
Effect on HbA_{1c}



**P* < .001

Weiss, et al. *Diabetes*. 1999;48(suppl 1):A12.

GLUCOSE MONITORING SYSTEMS - Telemetry

Consumer Product

- **“Real time” glucose readings**
- **Wireless communication from sensor to monitor**
- **High and low glucose alarms**
- **FDA panel pending**

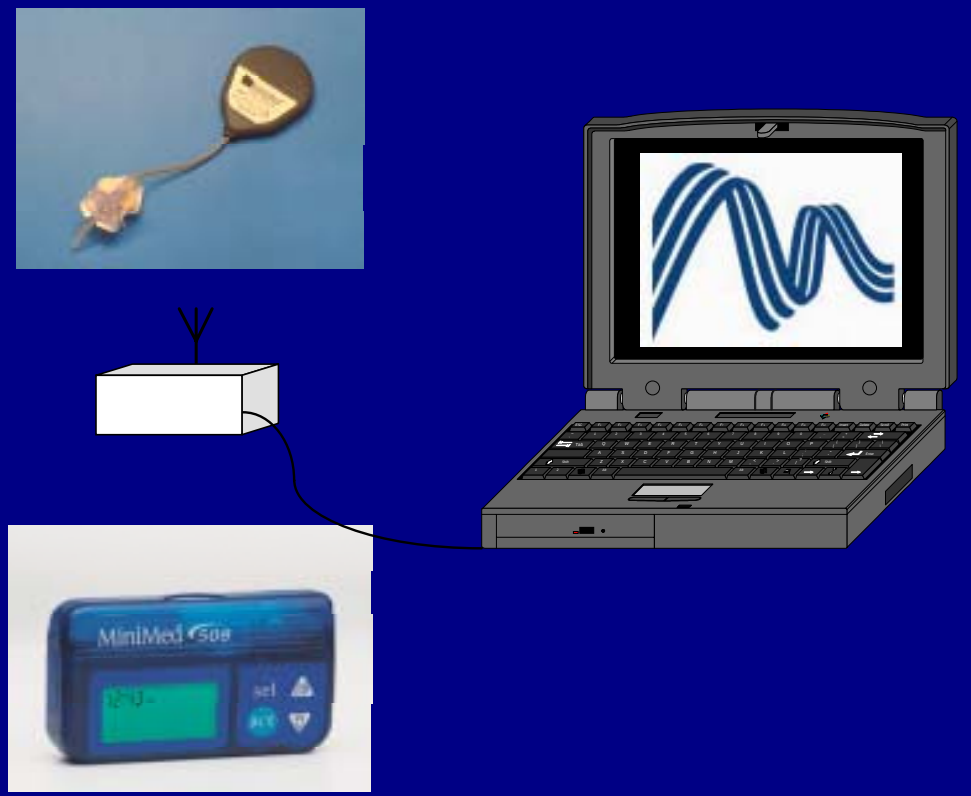
Closed-loop control using an external insulin pump and a subcutaneous glucose sensor

+

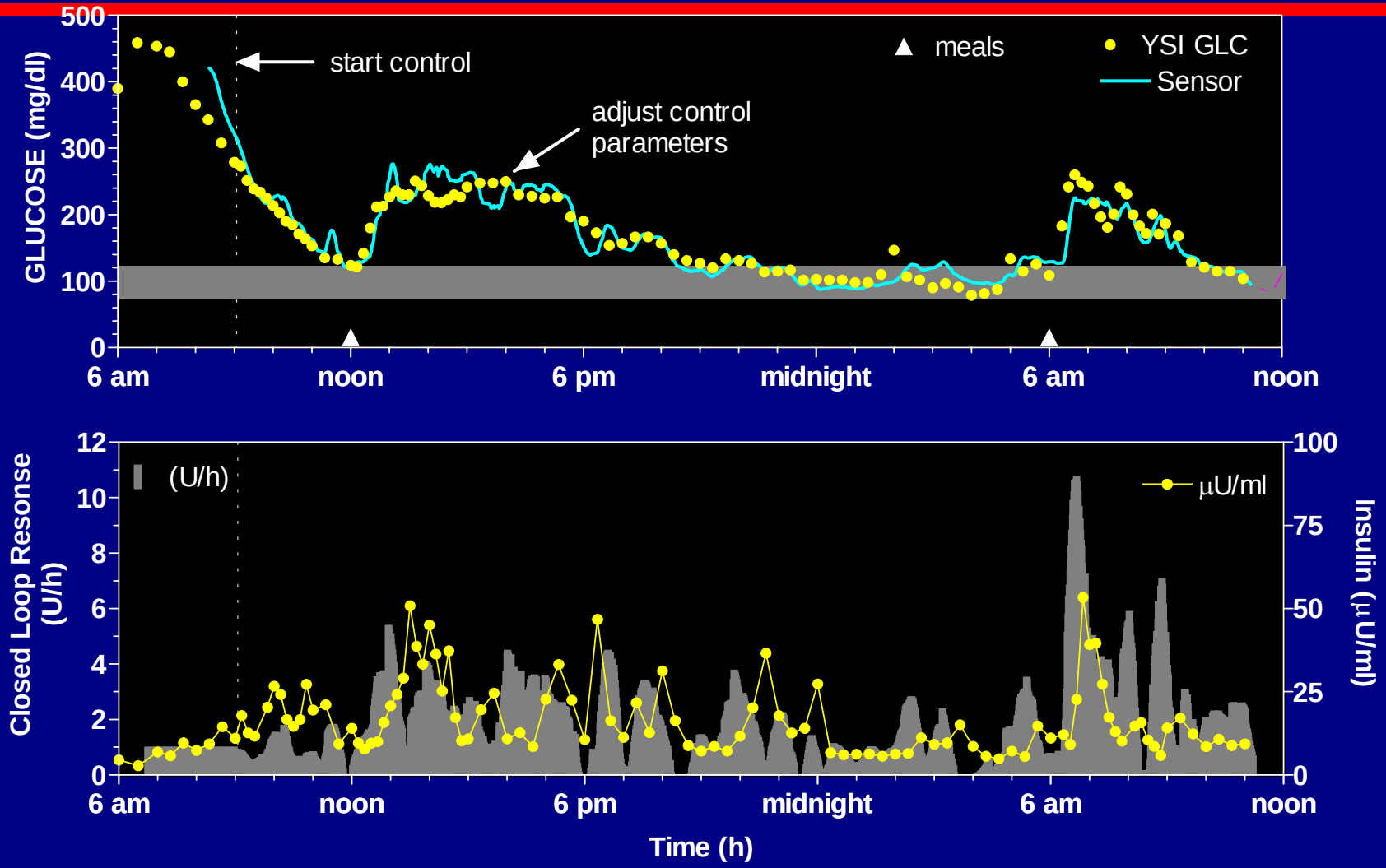
subcutaneous glucose sensor

Insulin infusion pump (currently MiniMed 508)

Closed-Loop Setup for Canine Studies



24-h Closed-Loop Control (diabetic canine)

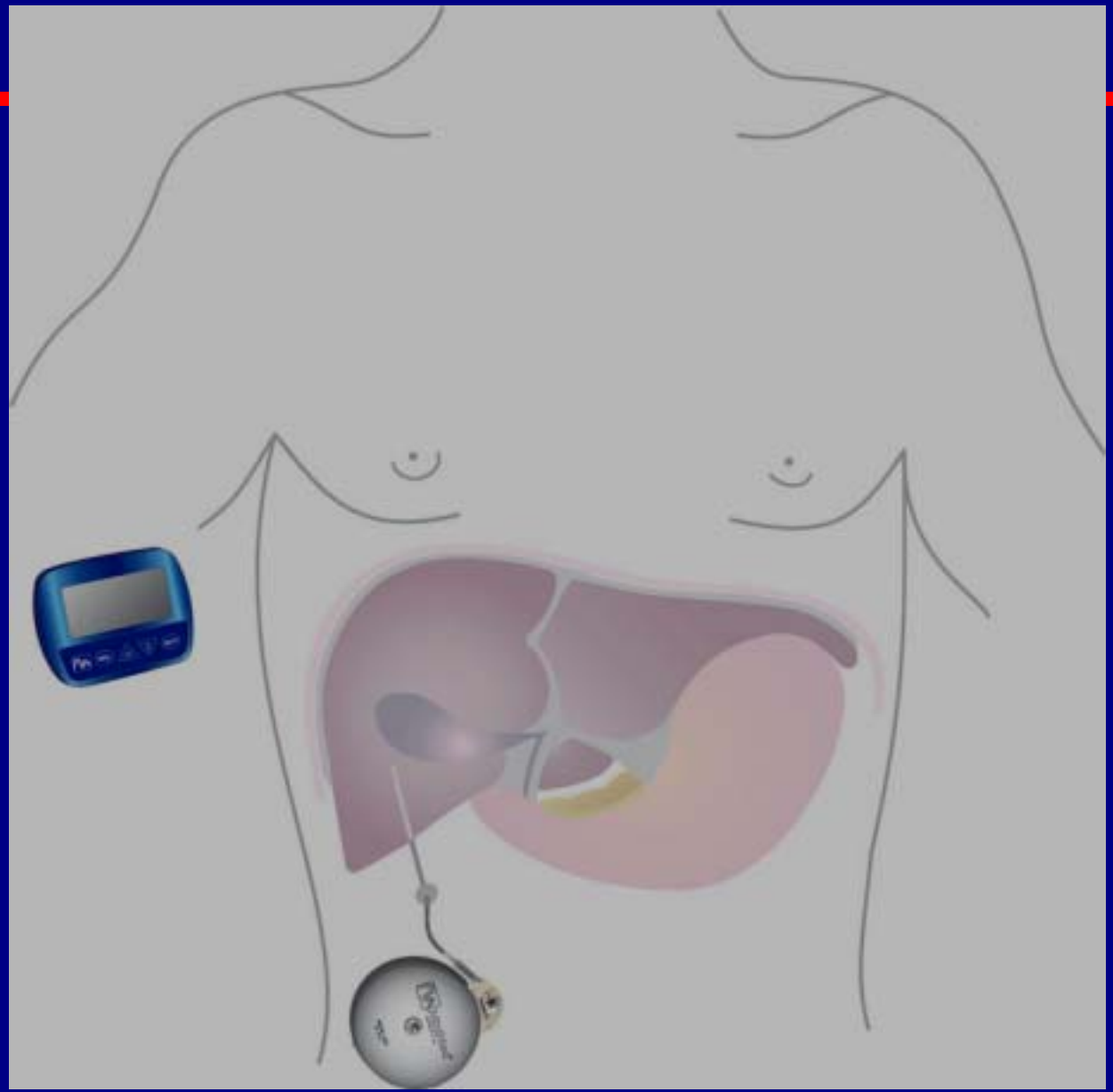


Implantable Pump

- Average HbA_{1c} 7.1%
- Hypoglycemic events reduce to 4 episodes per 100 pt-years

MiniMed 2007 System

Implantable Insulin Pump Placement



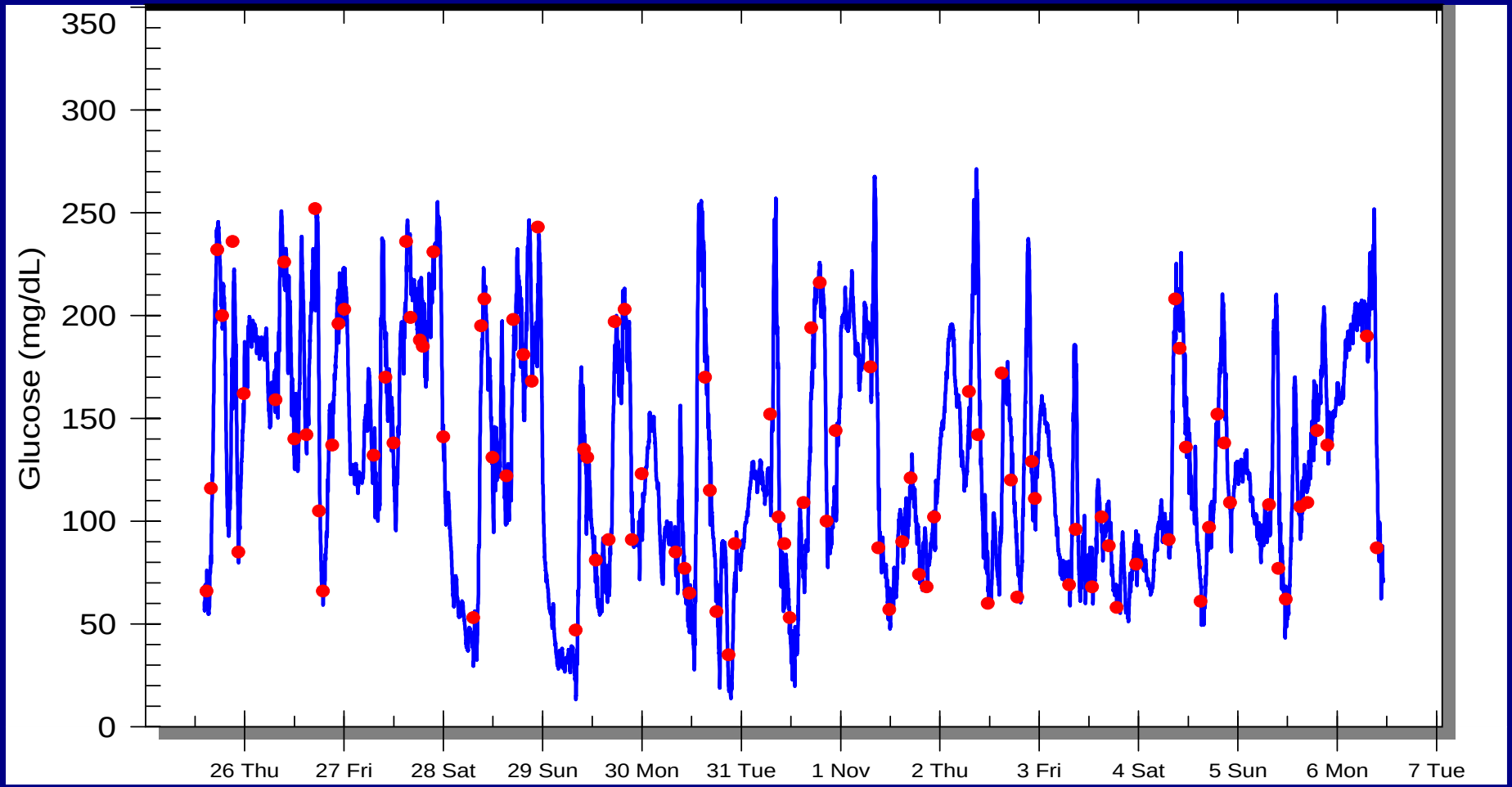
Implantable Insulin Pumps Indications for Use

- Diabetes out of control (frequent, rapid ρBG)
- Frequent hypoglycemic episodes
- Subcutaneous insulin absorption resistance
- Injection or infusion site reaction

Long-Term Glucose Sensor

LONG TERM IMPLANTABLE SYSTEM

Human Clinical Trial



Source: Medical Research Group, Inc.

Combine Pump and Sensor Technology

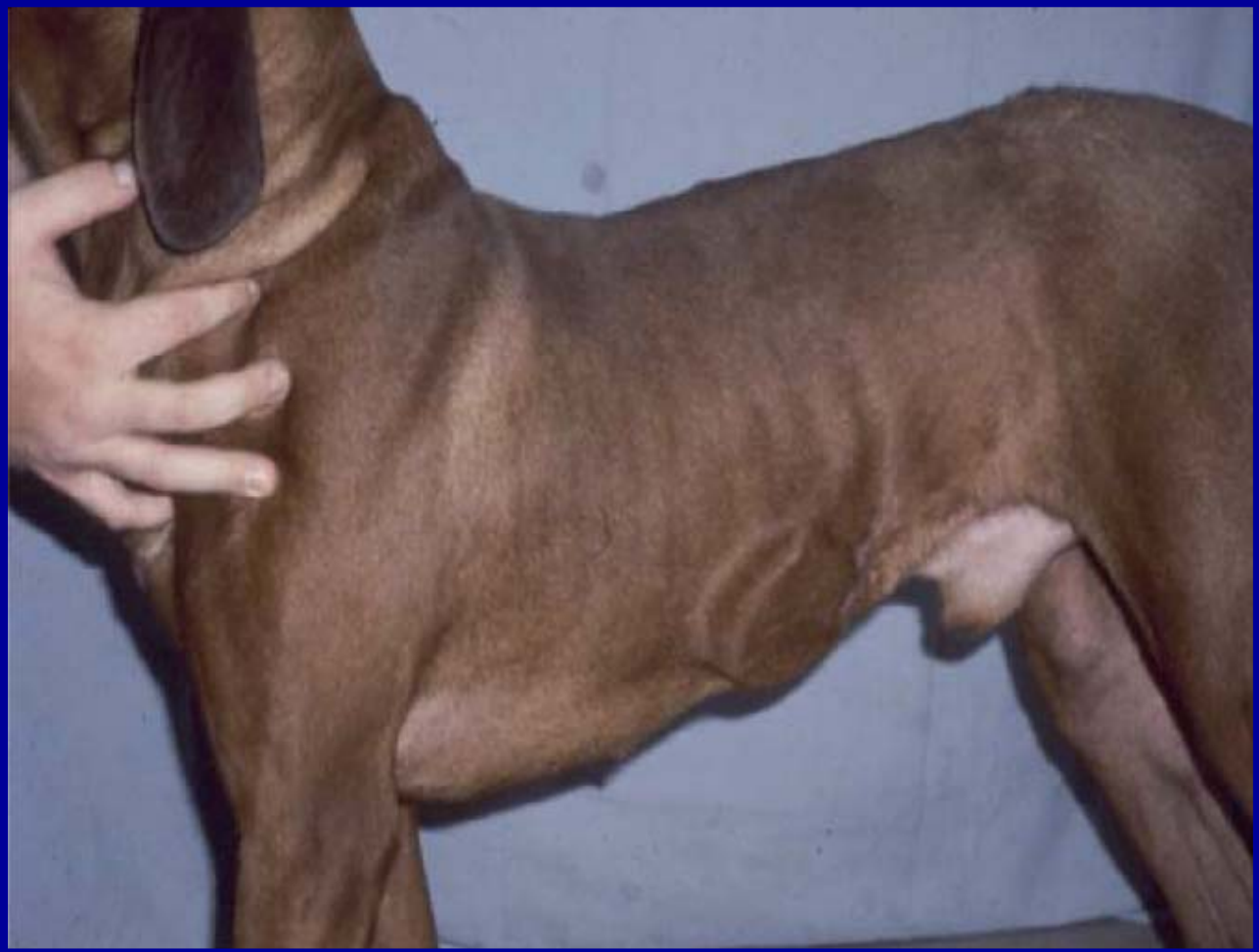
+

LTSS => Long Term Sensor System (“Open Loop Control”)

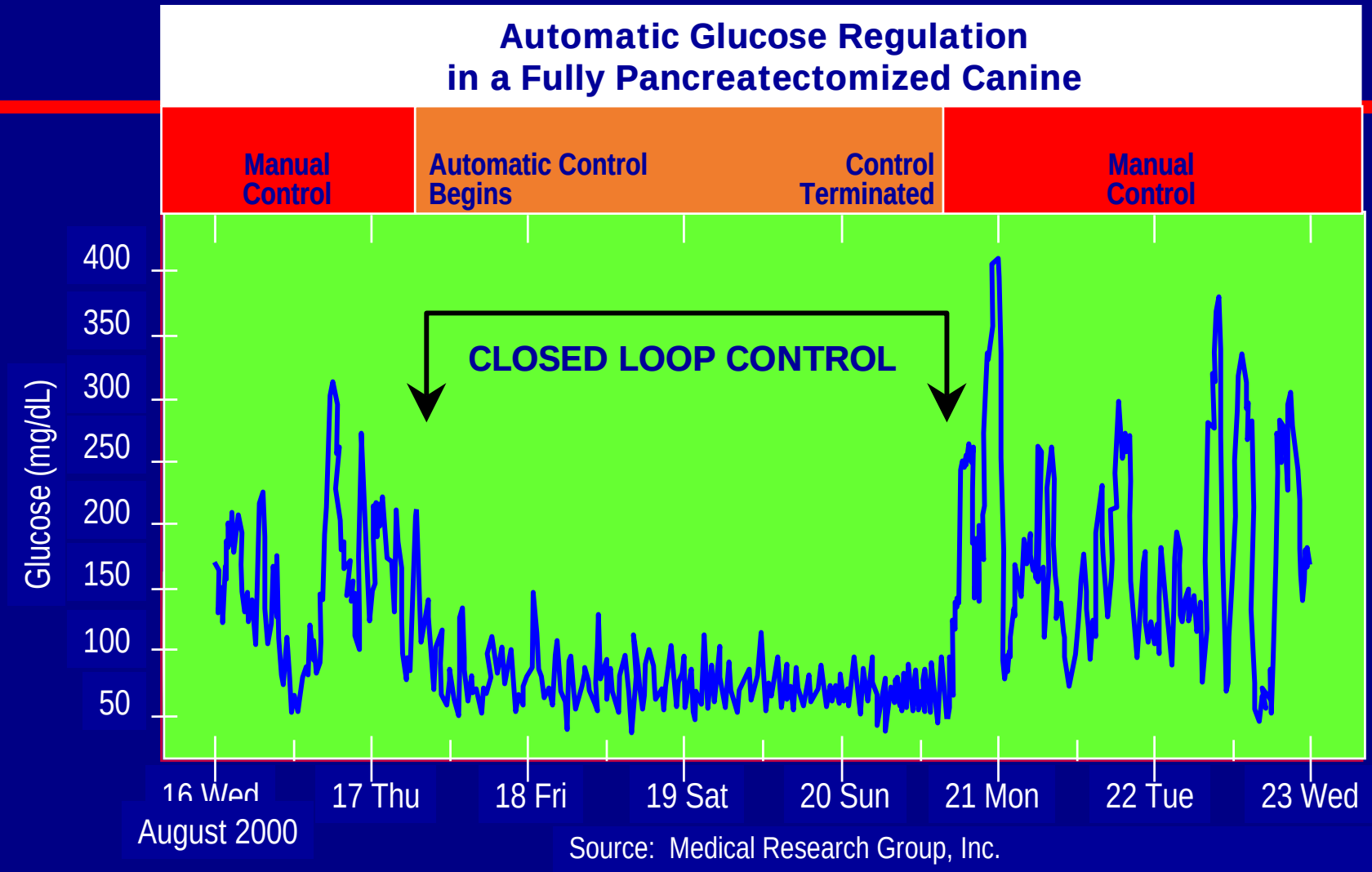
Using an RF Telemetry Link…...

Medtronic MiniMed's Implantable Biomechanical Beta Cell

Today's Reality
Open-Loop Glucose Control



LONG TERM IMPLANTABLE SYSTEM



Summary

- Insulin remains the most powerful agent we have to control diabetes
- When used appropriately in a basal/bolus format, near-normal glycemia can be achieved
- Newer insulins and insulin delivery devices along with glucose sensors will revolutionize our care of diabetes

Conclusion

Intensive therapy is the best way to treat patients with diabetes

QUESTIONS

- For a copy or viewing of these slides, contact
- WWW.adaendo.com
- Email: Minimedtalk@adaendo.com