

# **Role of Laboratory in Diabetes Care**

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# The Natural History of Diabetes

## Treatment Strategies

	Normal ↔ IGT	Diabetes Mellitus	Chronic Complications
<b>Treatment Strategy</b>	Prevent Diabetes	Treat Diabetes	Treat Complications
"Disease"	Progressive $\beta$ -cell Dysfunction	↑ Glucose	End-Organ Dysfunction
Clinical Detection	Rising Glucose	Glucose Above Risk Threshold	Varies
Treatment Goal	Stable $\beta$ -cell (Stable Glucose)	Low-Risk Glucose	Minimize Morbidity

# Tight Diabetes Control

## Post DCCT and UKPDS

Standardization

Continuity of care

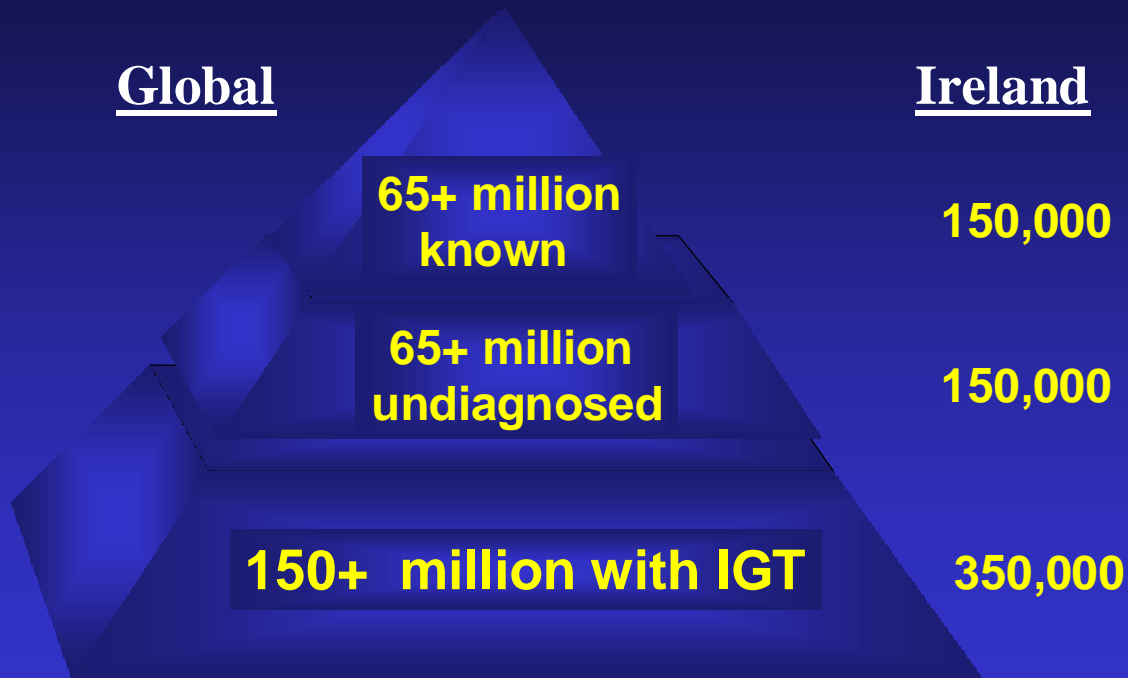
Self-care

Remote monitoring and intelligent titration algorithms

## **DIABETES PROJECTIONS:1995 - 2025 EUROPE**

- **Adult population will increase by 64%**
- **Number of people with diabetes will increase by 122%**

# TYPE 2 DIABETES & THE HIDDEN IGT EPIDEMIC



# Evolution of Type 2 Diabetes

Birth

Death

**NGT**

**IGT**

**DM**

**early**

**late**

'Normal'

**Insulin resistance**

Pre- Diabetes

**Insulin resistance**

**Kinetic defects**

**Delayed insulin secretion**

'Clinical' Diabetes

**Insulin resistance**

**Kinetic defects**

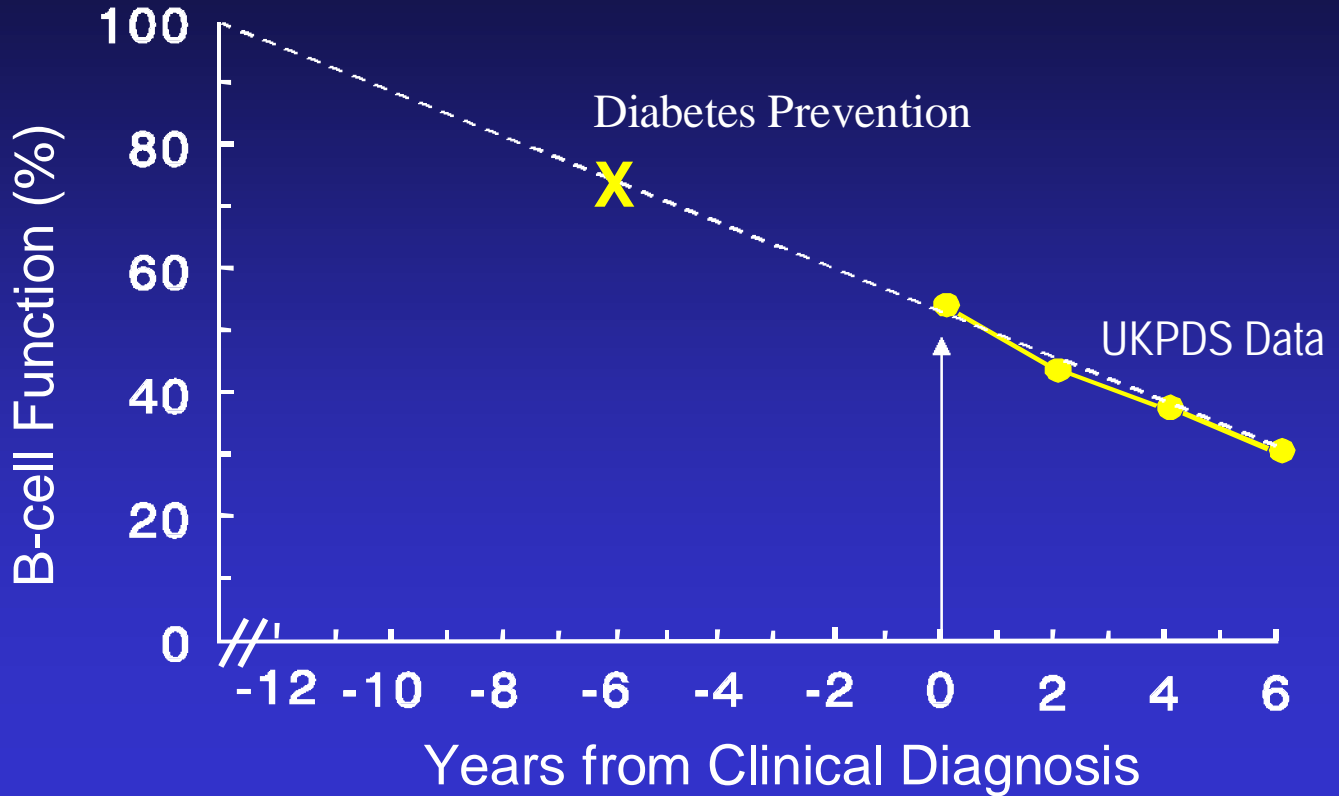
**Progressive loss of insulin secretion**

**Increased HGP**

*When do complications begin?*

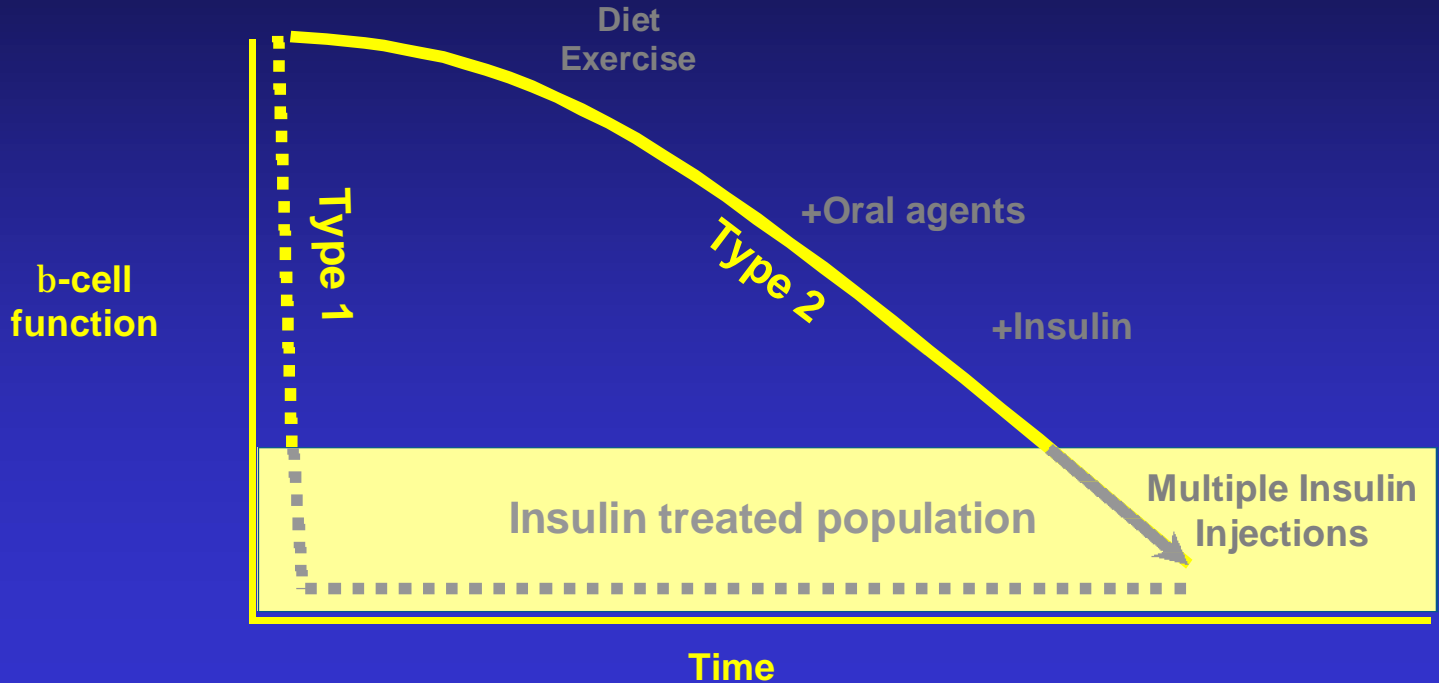
# Type 2 Diabetes

*Progressive Pancreatic B-cell Failure*



# Natural history of DM

An unmet medical need



# Key Laboratory Markers

HbA1C

Lipids

Urine albumin

plus

Insulin/C-peptide

Predictive markers: Antibodies, Genetics

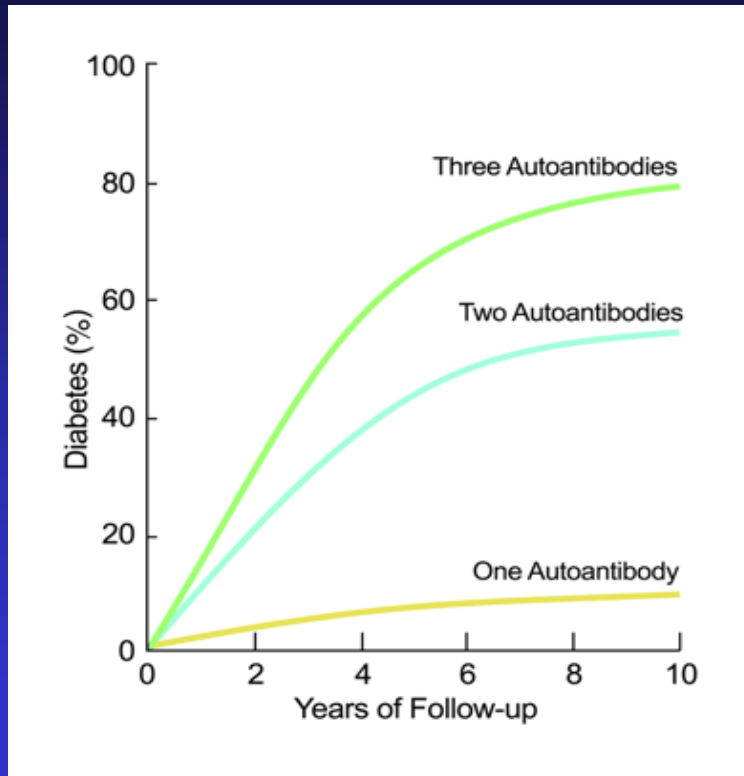
# Main autoantigens in Type 1 DM

	GAD65	IA-2	Insulin
Amino acid	585	979	51
Mol Wt	65,000	106,000	6,000
Locus	10p11	2q35	11p15
Cell Type	neuroendo	neuroendo	Islet beta
Found in	neuro vesic	Secr vesic	Secr vesic
Function	Glu to GABA	Inactive PTPase	Metabolic Regulation

# Autoantibody Frequency

- 70-80% of new Type 1 have GAD65
- 65-70% have IA-2
- Fewer have anti-insulin
- Age of subject: younger, higher freq
- GAD65 is the most stably expressed
- Controls: only 1% have these Ab's
- Type 2 Dm: 13% have GAD65

# Autoantibodies Predict Diabetes



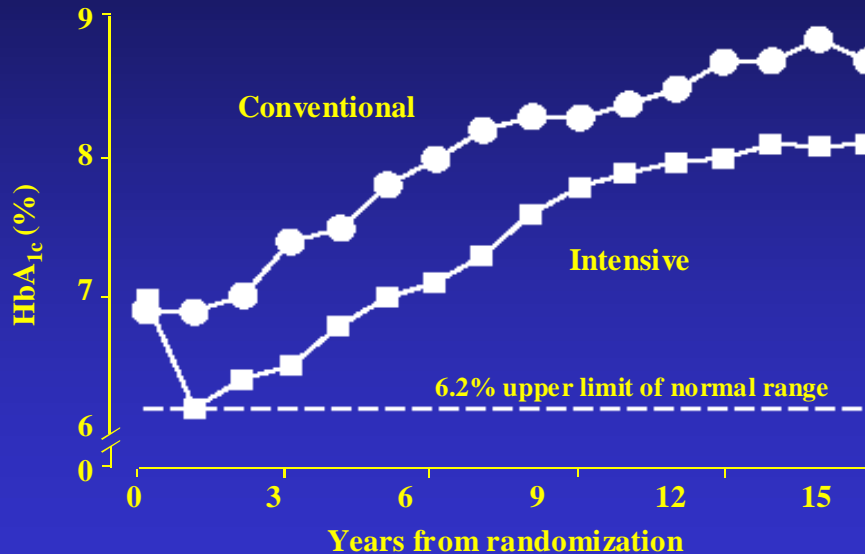
# LADA (GAD-positive) Common sub-phenotype

- ø Clinical presentation as Type 2 DM, non-Type 1
- ø Characterized by GAD-Abs, anti-insulin
- ø *13% of patients in our clinic* (excluding Type 1)
- ø Often clinically indistinguishable from Type 2

# Progression of Type 2 DM

Loss of insulin secretion

Increased insulin resistance



\*UK Prospective Diabetes Study (UKPDS) Group. *Lancet* 1998; **352**:837–53.

## UKPDS: EFFECTS OF INTENSIVE TREATMENT OF TYPE 2 DIABETES

Reduced HbA1c by 11% with intensive Rx (7.9 vs. 7.0%)

This leads to

12% decrease in any diabetes-related endpoint

25% decrease in microvascular endpoints

21% decrease in retinopathy at 12 years

33% decrease in microalbuminuria at 12 years

24% decrease in cataract

16% decrease in myocardial infarction (ns)

5% decrease in stroke (ns)

# Poor Diabetic Control is a Major Cause of Heart Attack, Stroke, Blindness, Loss of Legs and Feet and Kidney Failure

Name		Sex		Date of DM	
Record		Date of Birth		Year of DM onset	

Date Quarterly	Weight (kg)	Blood Pressure Near 120/80	HbA1c Less than 6%	Lipid Profile				UAE <30 mg/24hr
				TC<5.2	LDL<3.4	HDL>1.0	TG<2.0	

Year	Eyes	Kidney	Nerves	Vessels	Feet

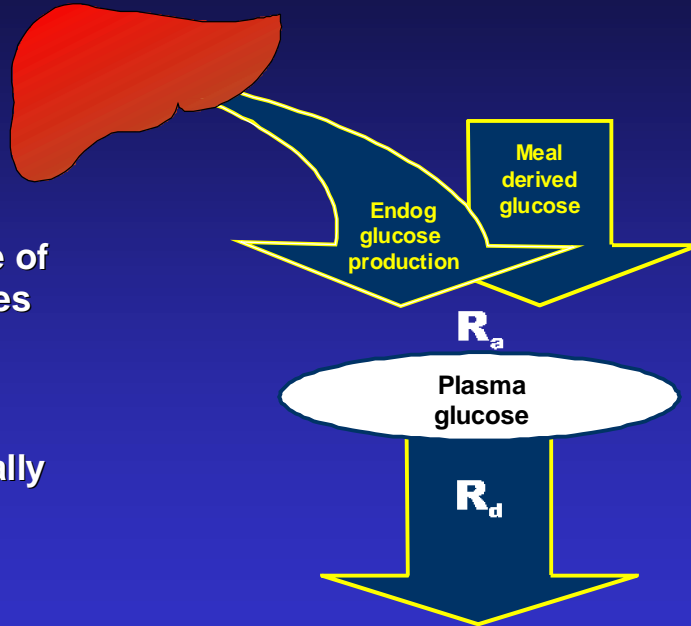
## Annual Examination

- 0=nondetectable
- 1=present
- 2=moderate
- 3=severe

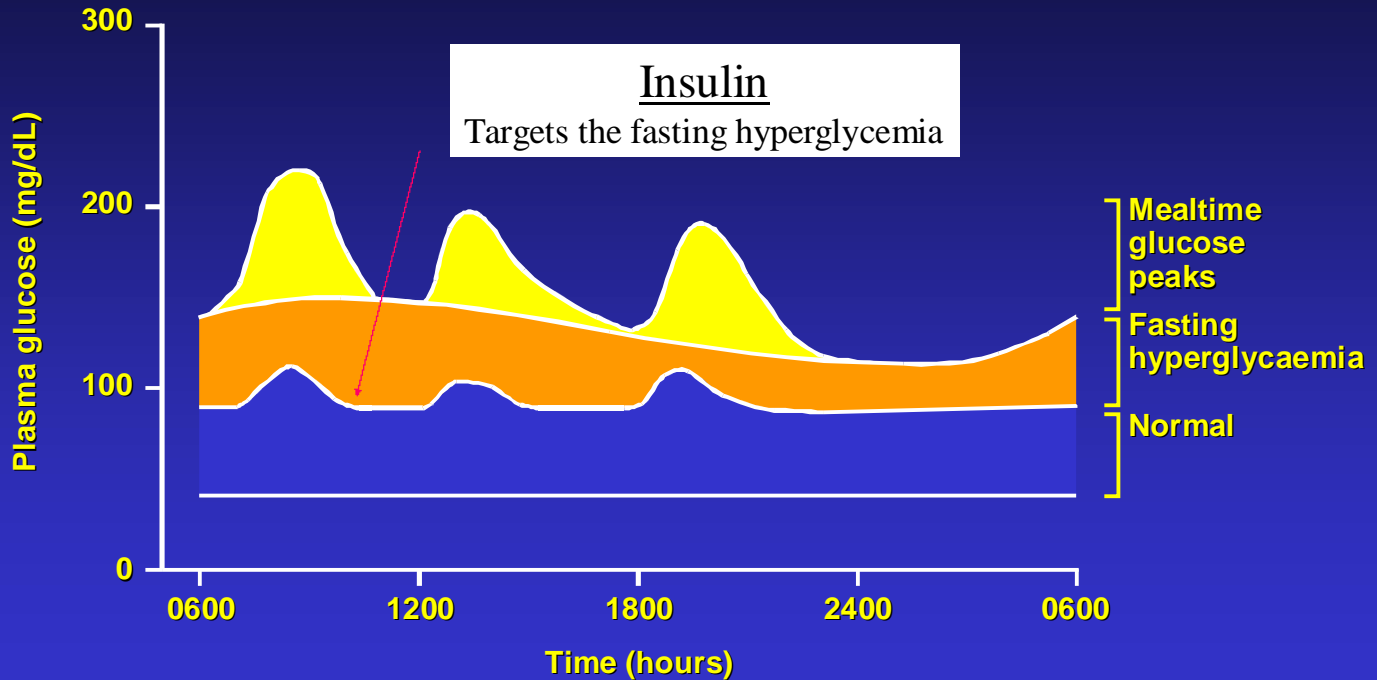
# Plasma glucose: $R_a$ vs $R_d$

Plasma glucose concentration changes only if rate of appearance ( $R_a$ ) does not match glucose disposal rate ( $R_d$ )

$R_a$  and  $R_d$  are normally closely matched

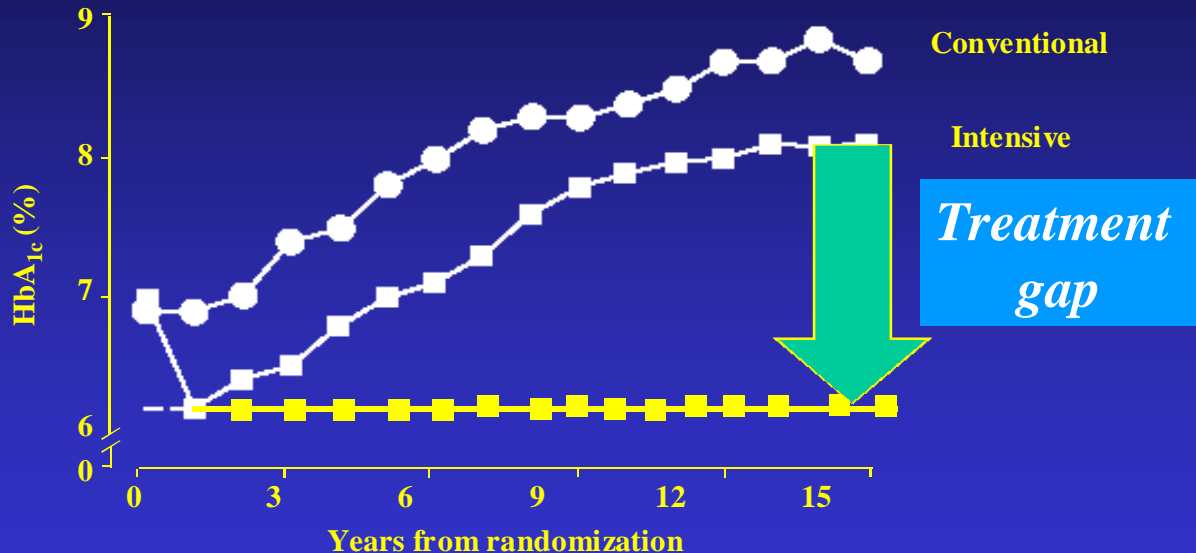


# HbA1c = fasting + postprandial



# Modern Treatment Target

## Sustained near-normoglycemia



# GAD+ and GAD- Type 2 DM

	GAD -	GAD +	P
Age	52.7±1.8	54.5 ±4.5	NS
Gender	7/5	7/5	7/5
HbA1C	7.6 ±0.3	7.9 ±0.3	NS
Duration	3.4 ±0.6	4.5 ±1.3	NS
Weight	91 ±2	77 ±3	0.003
Height	1.67	1.70	NS
BMI	32.9 ±1.3	26.7 ±1.2	0.002
WHR	1.01/0.95	0.92/0.85	0.01/0.04
BP	134/80	142/81	NS