Salzburg Diabetes Lecture

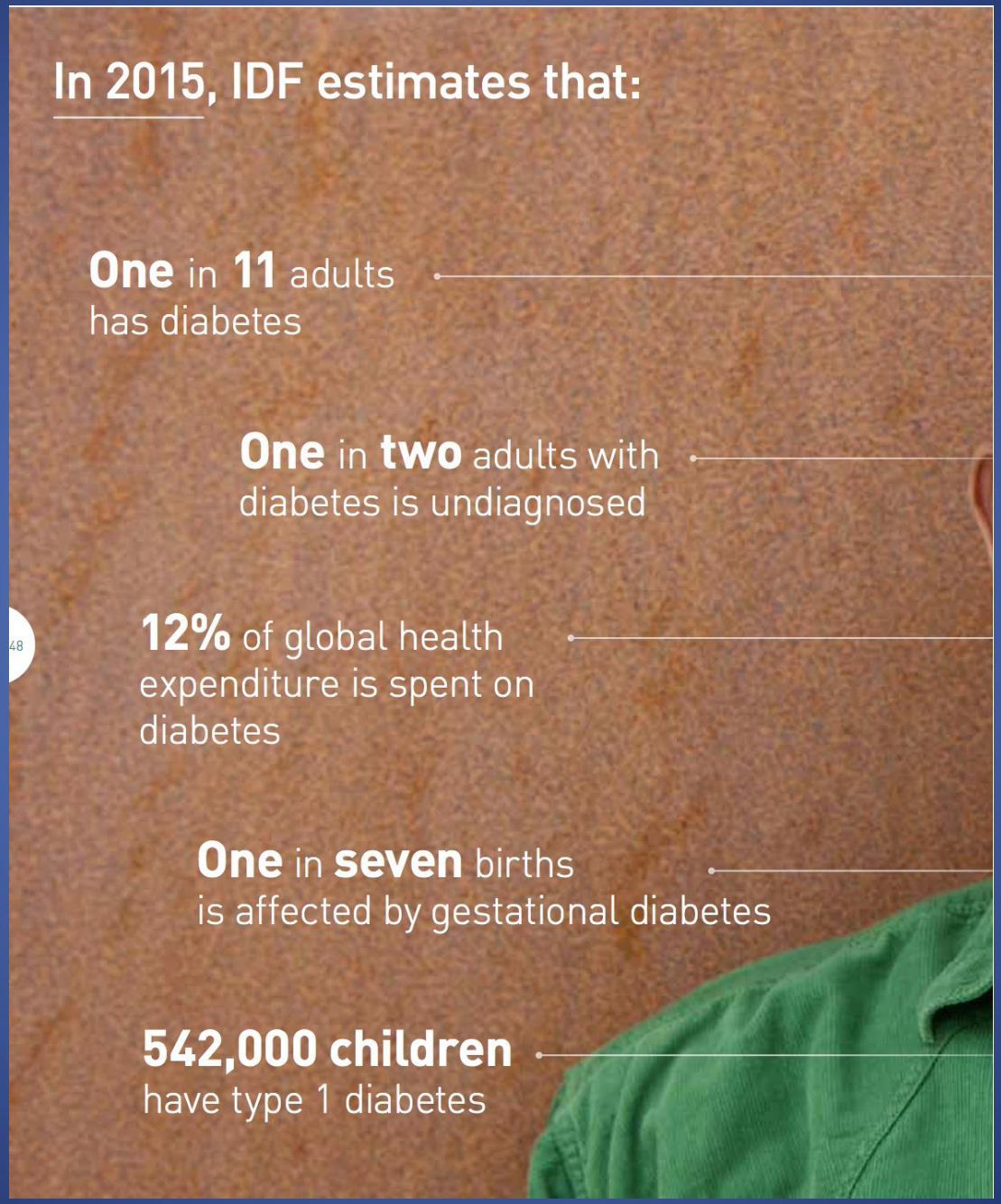
Type 1 Diabetes Update

Robin Goland, MD

May, 2017

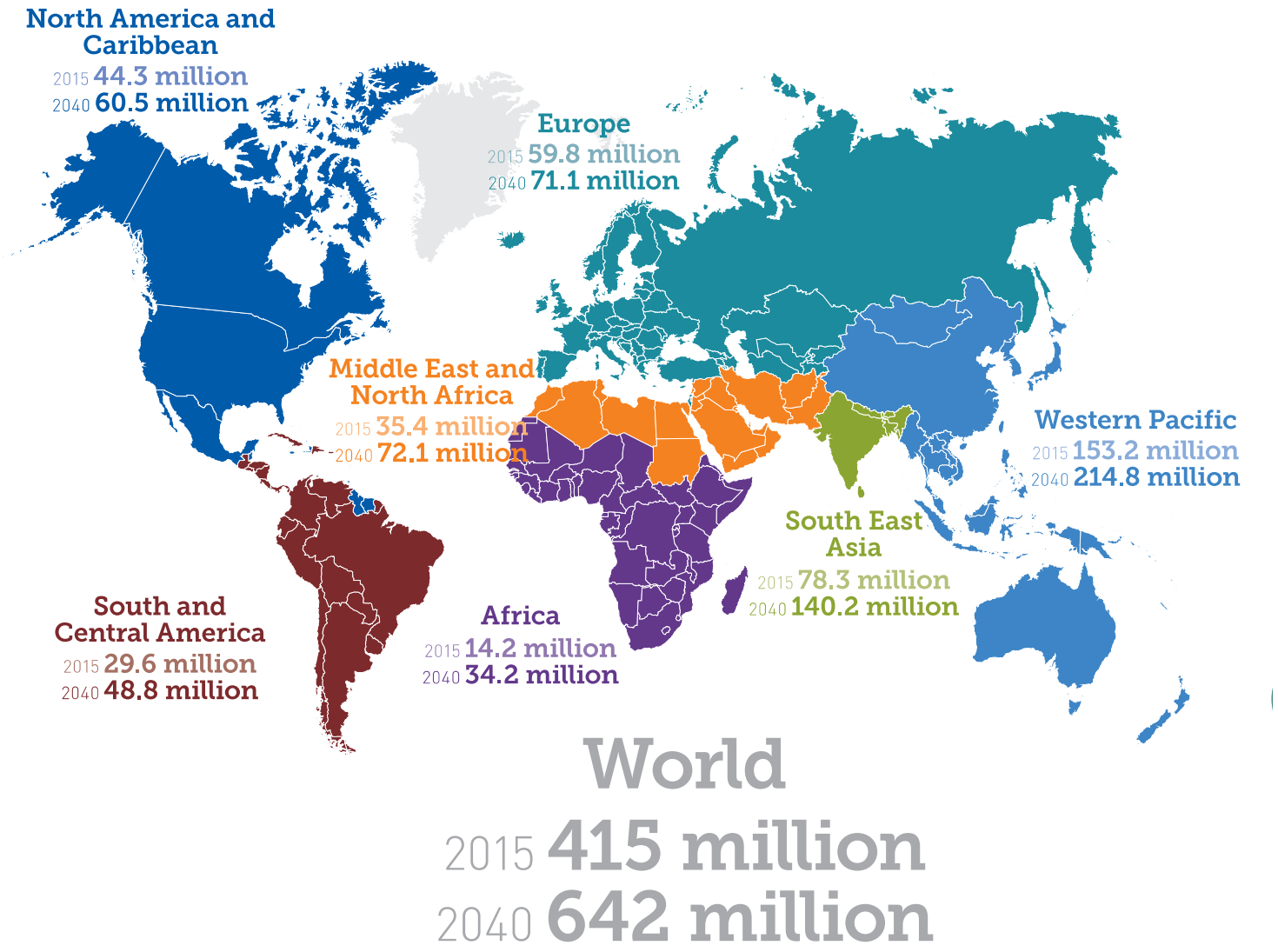
Type 1 Diabetes

- Epidemiology
- Pathophysiology
- Current Treatment and Outcomes
- Future Directions: Treatment and Prevention



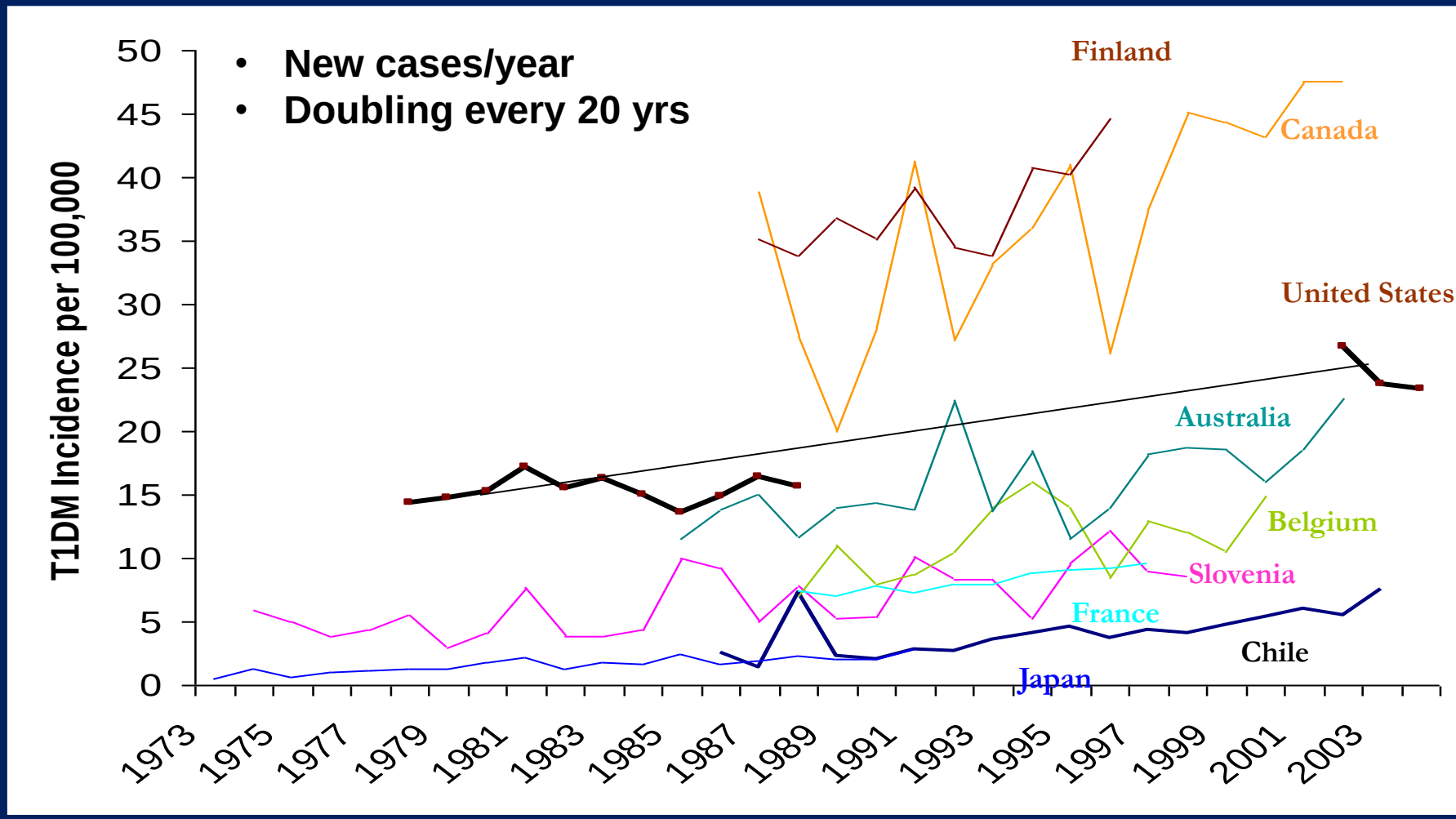
IDF Atlas 2015

Estimated number of people with diabetes worldwide and per region in 2015 and 2040 (20-79 years)



IDF Atlas 2015

Worldwide Incidence Trends



Vehik & Dabelea. DMRR 27: 3-13, 2011

Childhood Diabetes Trends Worldwide

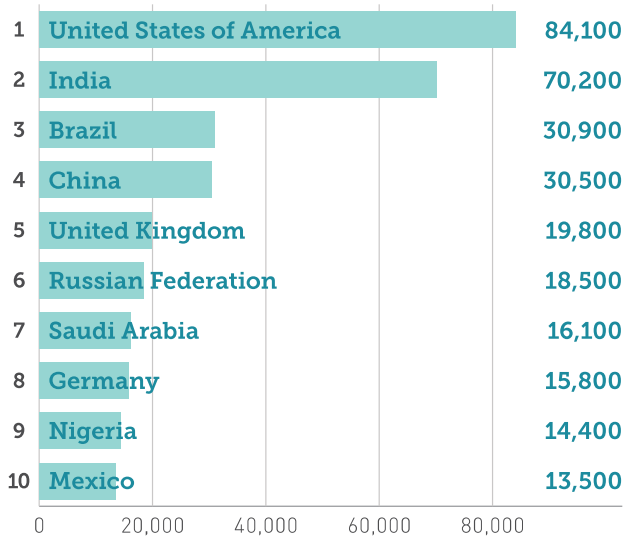
Diabetes in children

Whilst type 1 diabetes is less common, it is still increasing by around 3% every year, particularly among children. Around 86,000 children develop type 1 diabetes each year and when insulin is not available, the life expectancy for a child with type 1 diabetes is very short. The IDF Life For A Child programme supplies insulin to 17,000 children in 46 countries.

In 2015 the number of **children** with type 1 diabetes exceeded **half a million** for the first time

Children with diabetes

Top 10 countries for number of **children** with type 1 diabetes (0-14 years)



Number of children with type 1 diabetes worldwide 542,000

IDF Atlas 2015

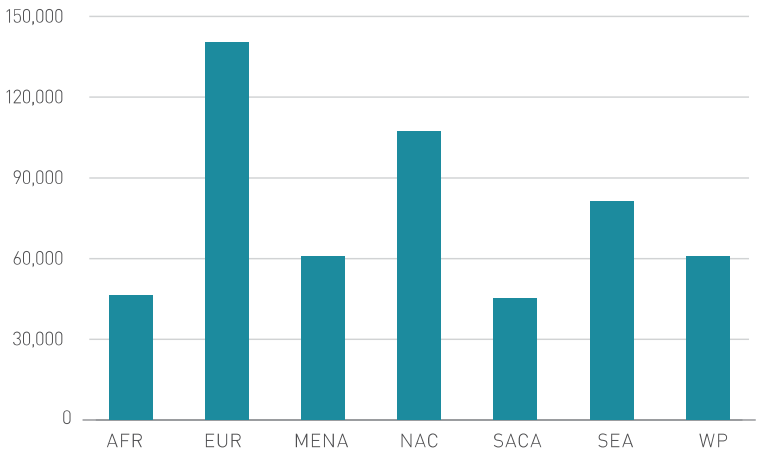
Childhood Diabetes Trends Worldwide

Table 3.9 Global estimates of type 1 diabetes in children (<15 years) for 2015

Child population (< 15 years)	1.9 billion
Type 1 diabetes in children (< 15 years)	
Number of children with type 1 diabetes	542,000
Number of new type 1 diabetes cases per year	86,000
Annual increase in incidence	3%*

* Estimate from the *Diabetes Mondiale study (DIAMOND)*[24], the *Europe and Diabetes study (EURODIAB)*[25].

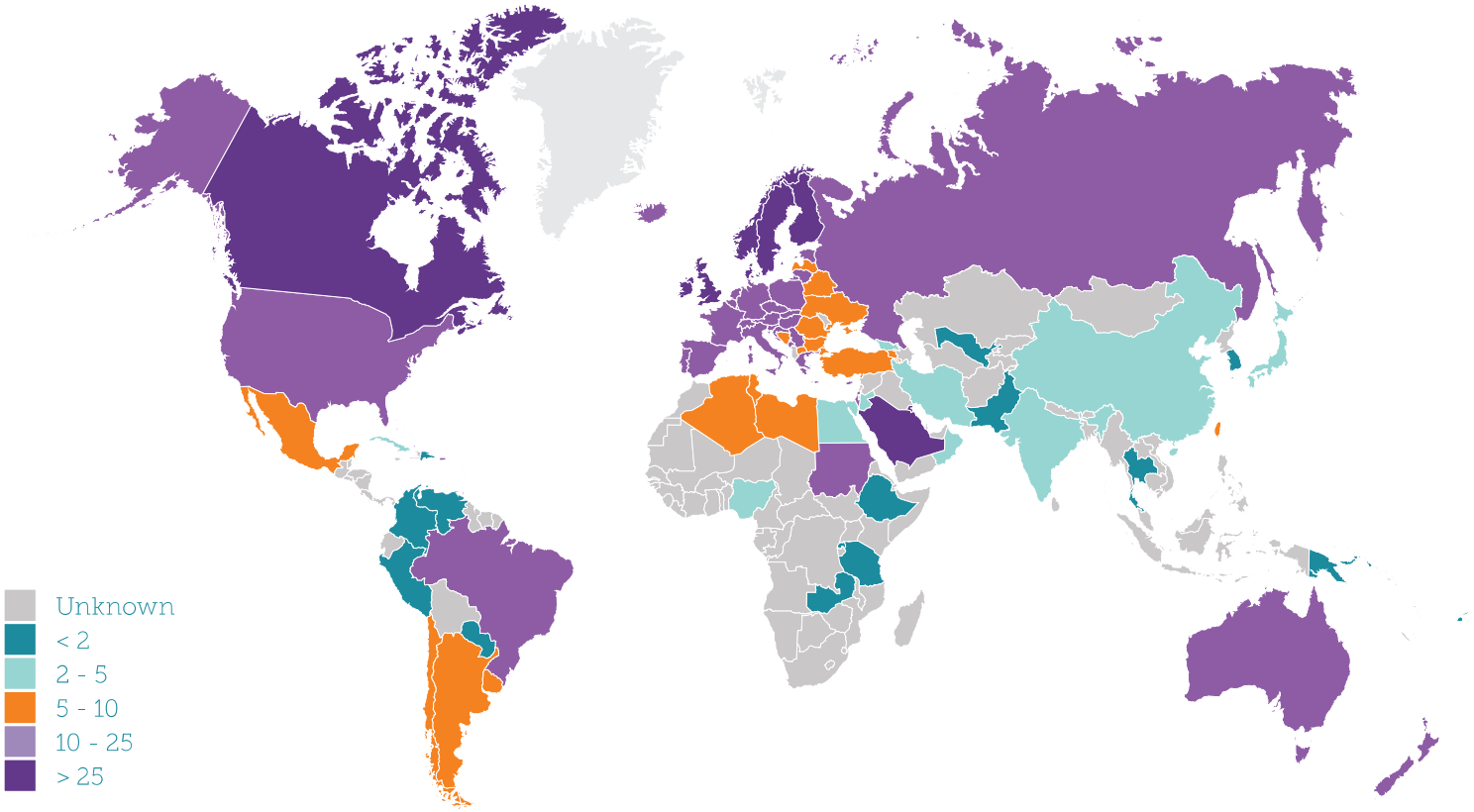
Figure 3.6 Estimated number of children (< 15 years) with type 1 diabetes by IDF region, 2015



IDF Atlas 2015

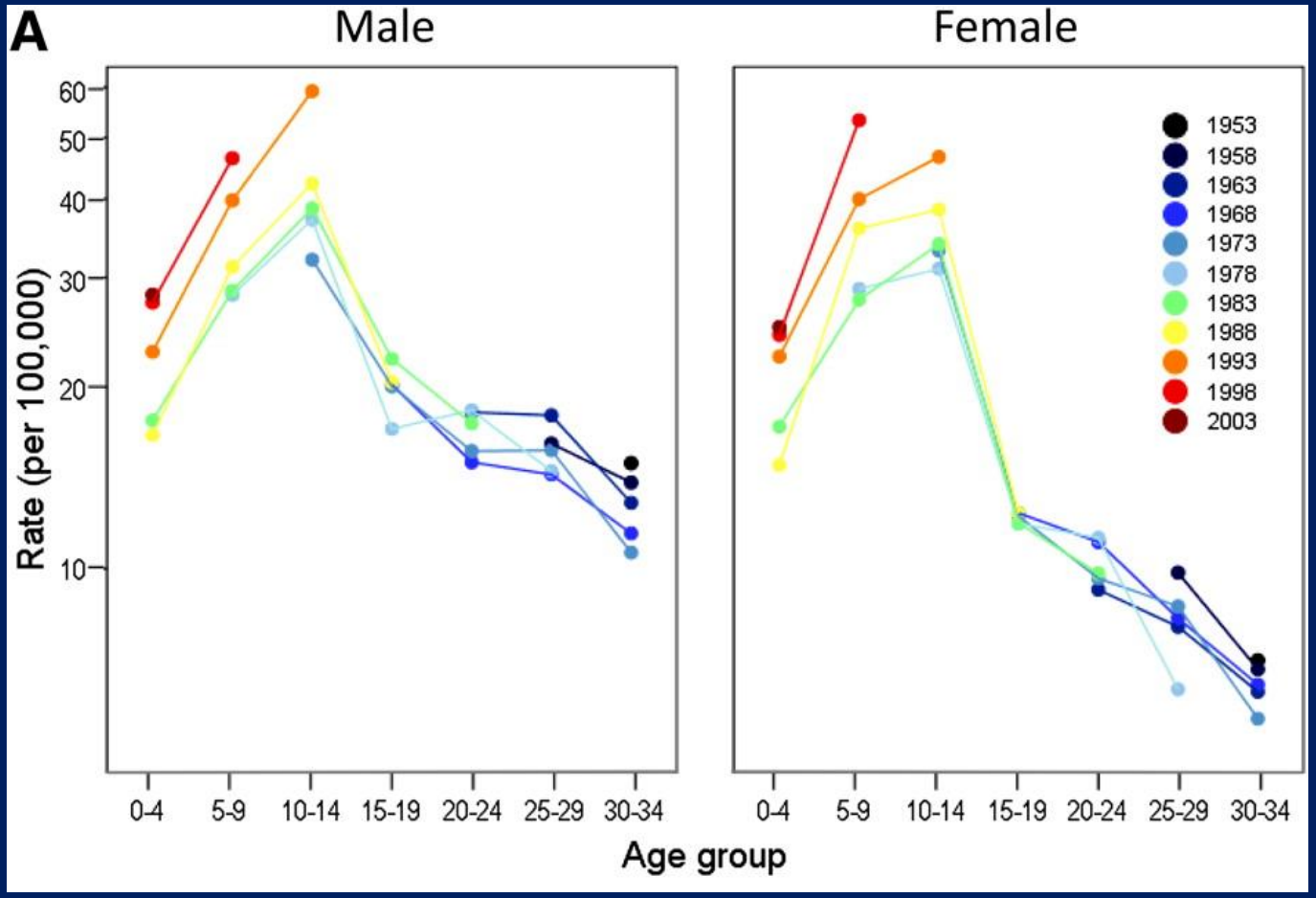
Childhood Diabetes Trends Worldwide

Map 3.9 Estimated new cases of type 1 diabetes (< 15 years) per 100,000 children per year, 2015



IDF Atlas 2015

T1D Incidence Rate



Changing Face of T1D

- Increasing numbers of children with new onset T1D
- Up to 1/3 may be > 18 years of age at T1D onset
- Fewer with high risk HLA alleles

Dahlquist G G Dia Care 2011;34:1754-1759

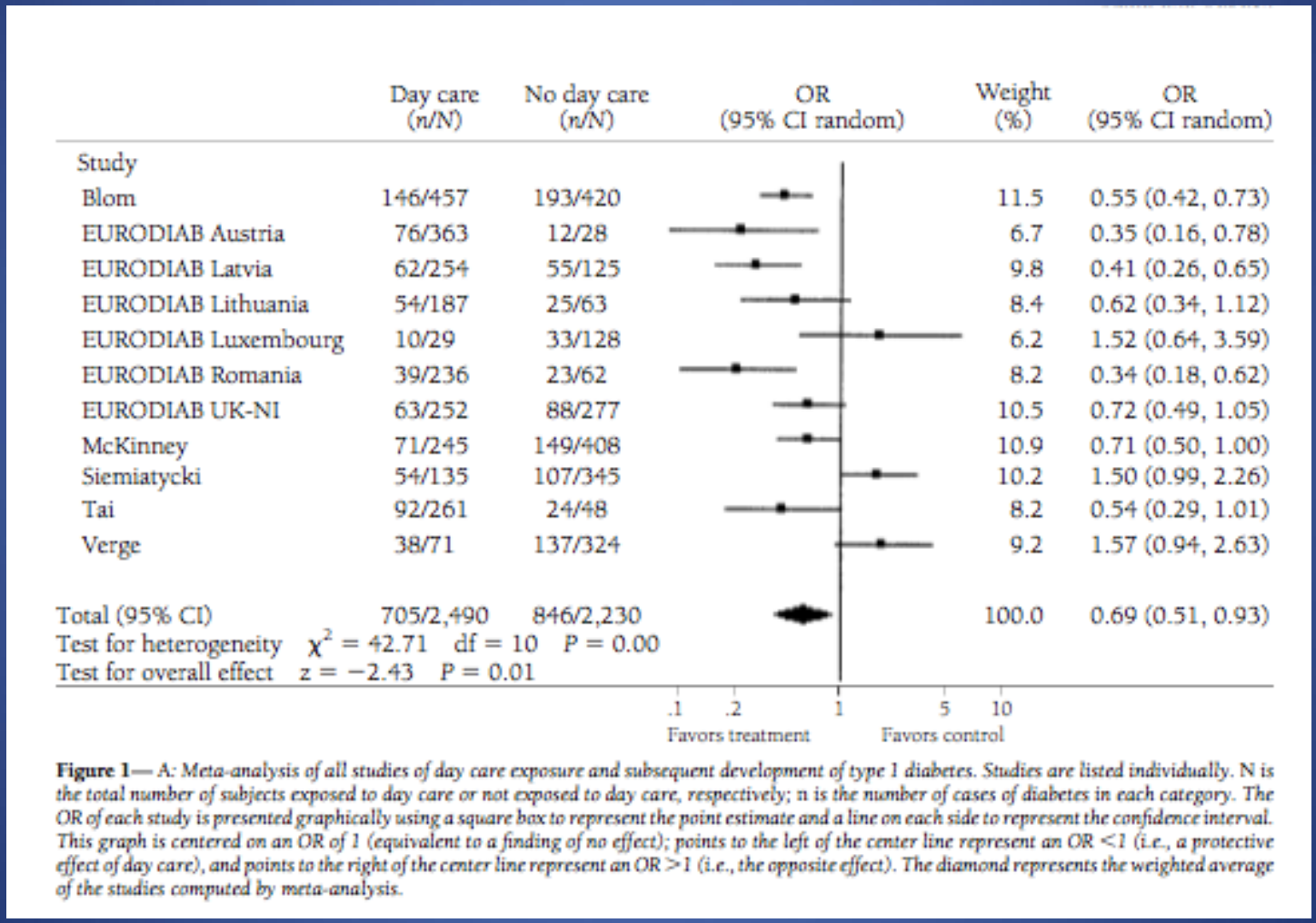
Genetic Risk for T1D

- HLA accounts for 30-50% of risk (chromosome 6)
- Greatest association with HLA class II haplotypes DRB1*0301-DQB1*0201 (DR3-DQ2) and DRB1*0401-DQB1*0302 (DR4-DQ8)
- Genotype associated with the highest risk for T1D is the heterozygous DR3/4 genotype.
- HLA class II DRB1*1501 and DQA1*0102-DQB1*0602 confer disease resistance
- Highest non-HLA genetic contribution from INS, PTPN22, CTLA4, and IL2RA genes
- Relatives have 10-100x risk of T1D than general population highlighting genetic risk

Environmental Risk for T1D

- Identical twins only have 70% concordance, highlighting environmental component of risk
- Family history of T1D only present in 15% patients
- NIH TEDDY Study investigating environmental etiologies to TID

Potential Environmental Component of T1D

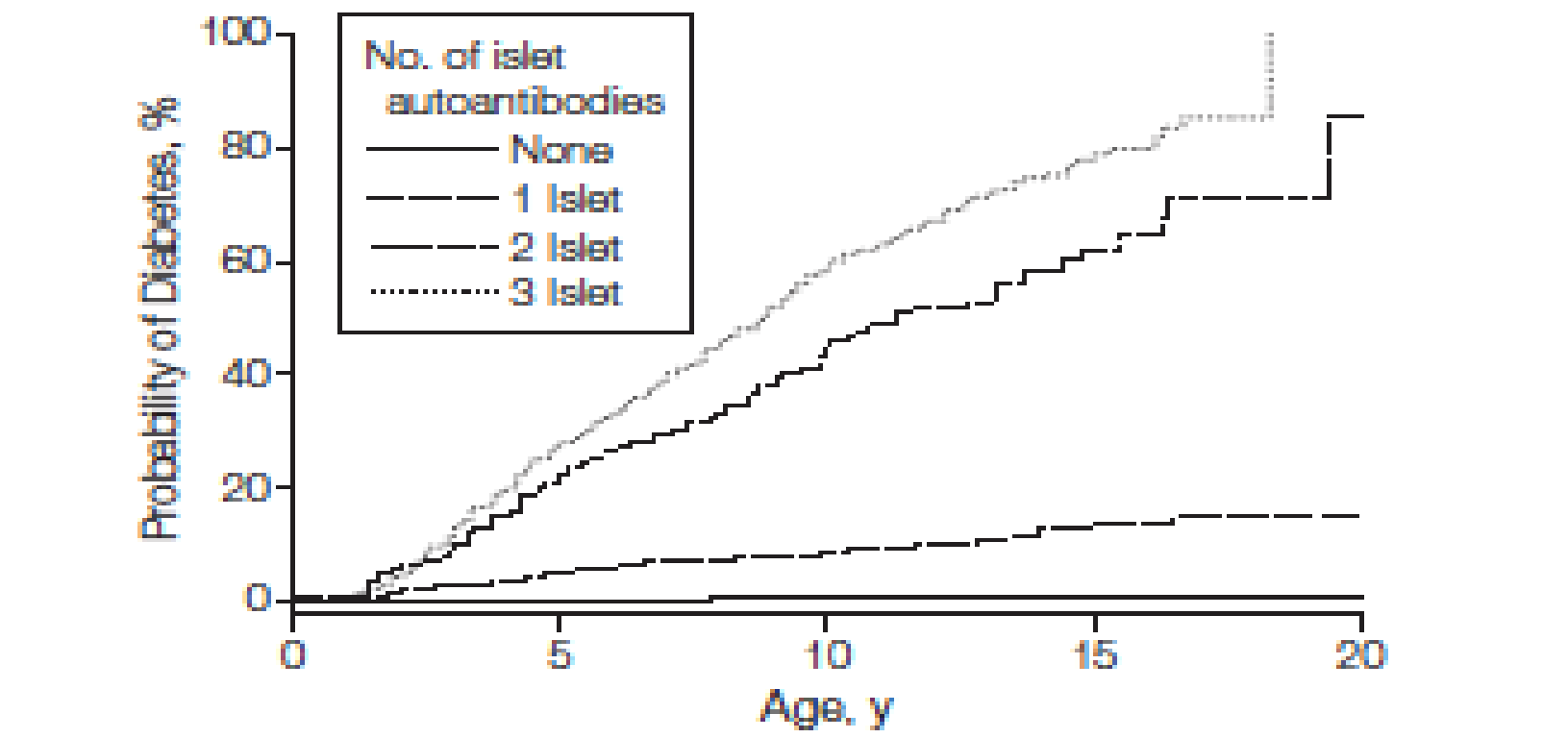


Study	Day care (*n*/*N*)	No day care (*n*/*N*)	OR (95% CI random)	Weight (%)	OR (95% CI random)
Blom	146/457	193/420		11.5	0.55 (0.42, 0.73)
EURODIAB Austria	76/363	12/28		6.7	0.35 (0.16, 0.78)
EURODIAB Latvia	62/254	55/125		9.8	0.41 (0.26, 0.65)
EURODIAB Lithuania	54/187	25/63		8.4	0.62 (0.34, 1.12)
EURODIAB Luxembourg	10/29	33/128		6.2	1.52 (0.64, 3.59)
EURODIAB Romania	39/236	23/62		8.2	0.34 (0.18, 0.62)
EURODIAB UK-NI	63/252	88/277		10.5	0.72 (0.49, 1.05)
McKinney	71/245	149/408		10.9	0.71 (0.50, 1.00)
Siemiatycki	54/135	107/345		10.2	1.50 (0.99, 2.26)
Tai	92/261	24/48		8.2	0.54 (0.29, 1.01)
Verge	38/71	137/324		9.2	1.57 (0.94, 2.63)
Total (95% CI)	705/2,490	846/2,230		100.0	0.69 (0.51, 0.93)
Test for heterogeneity	$\chi^2 = 42.71$	df = 10	$P = 0.00$		
Test for overall effect	$z = -2.43$	$P = 0.01$			

Figure 1— *A: Meta-analysis of all studies of day care exposure and subsequent development of type 1 diabetes. Studies are listed individually. N is the total number of subjects exposed to day care or not exposed to day care, respectively; n is the number of cases of diabetes in each category. The OR of each study is presented graphically using a square box to represent the point estimate and a line on each side to represent the confidence interval. This graph is centered on an OR of 1 (equivalent to a finding of no effect); points to the left of the center line represent an OR <1 (i.e., a protective effect of day care), and points to the right of the center line represent an OR >1 (i.e., the opposite effect). The diamond represents the weighted average of the studies computed by meta-analysis.*

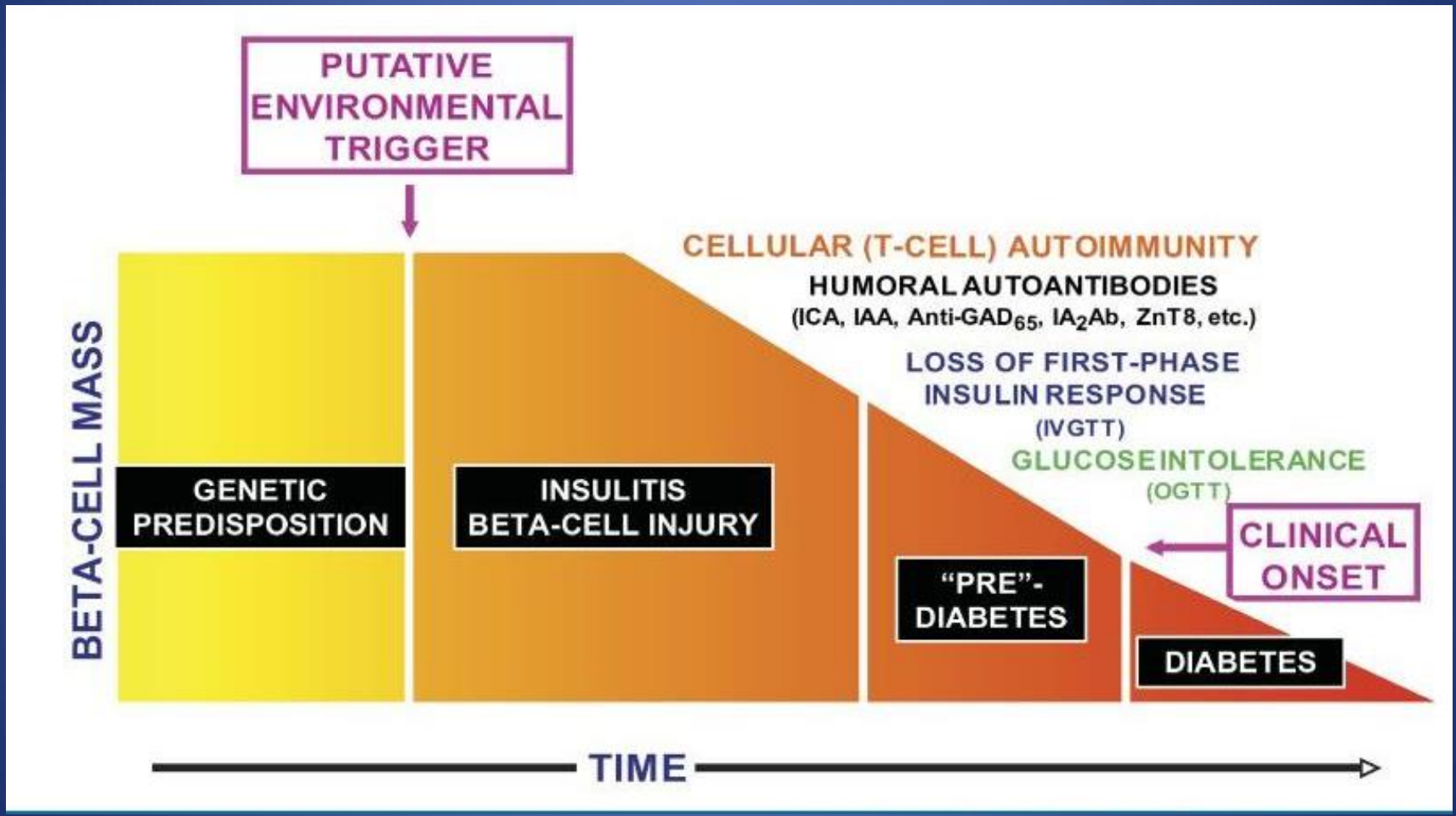
Kaila 2001 Diabetes Care

Multiple Islet Autoantibodies and Progression to T1D

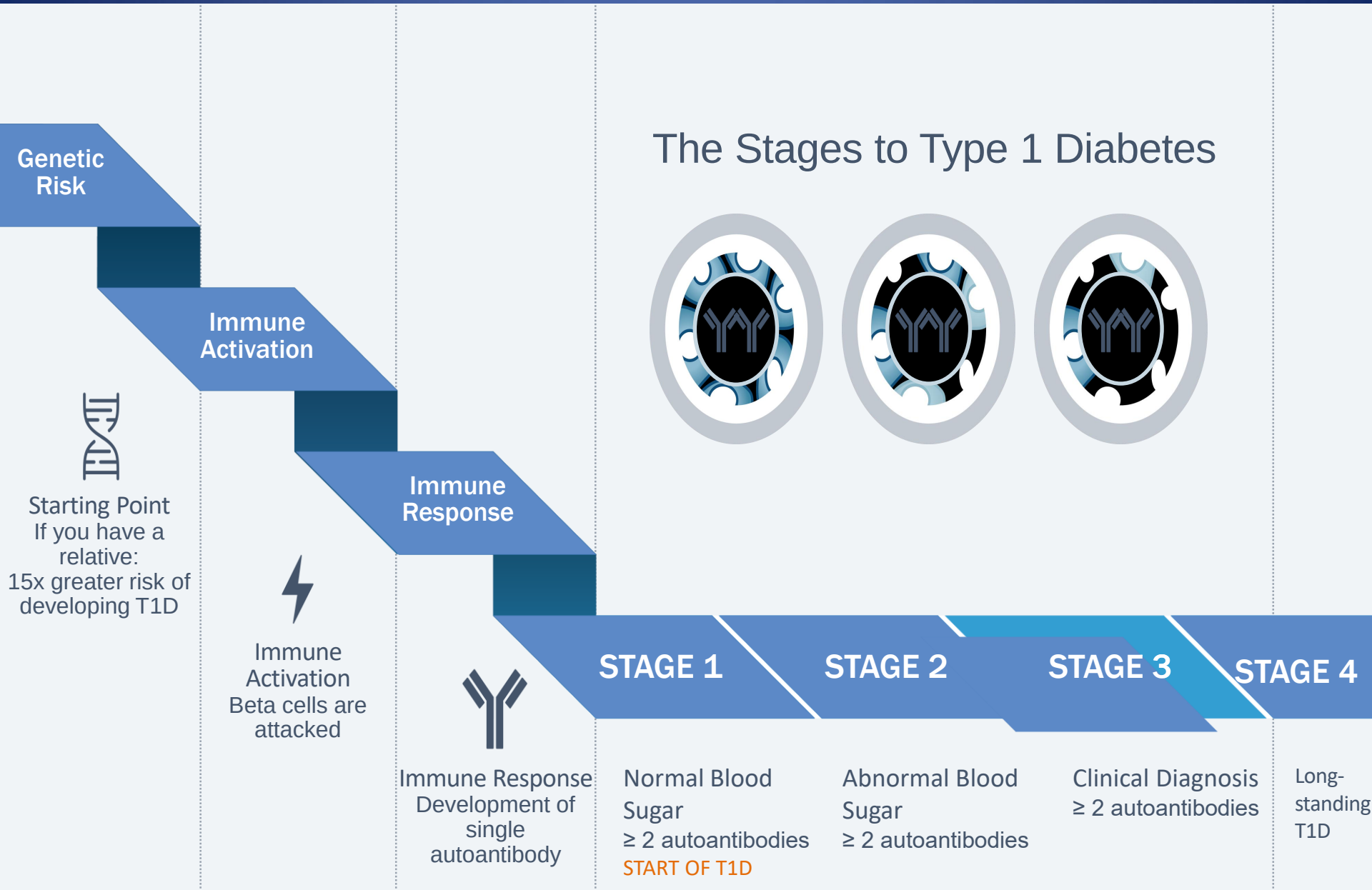


Ziegler, JAMA, 2013

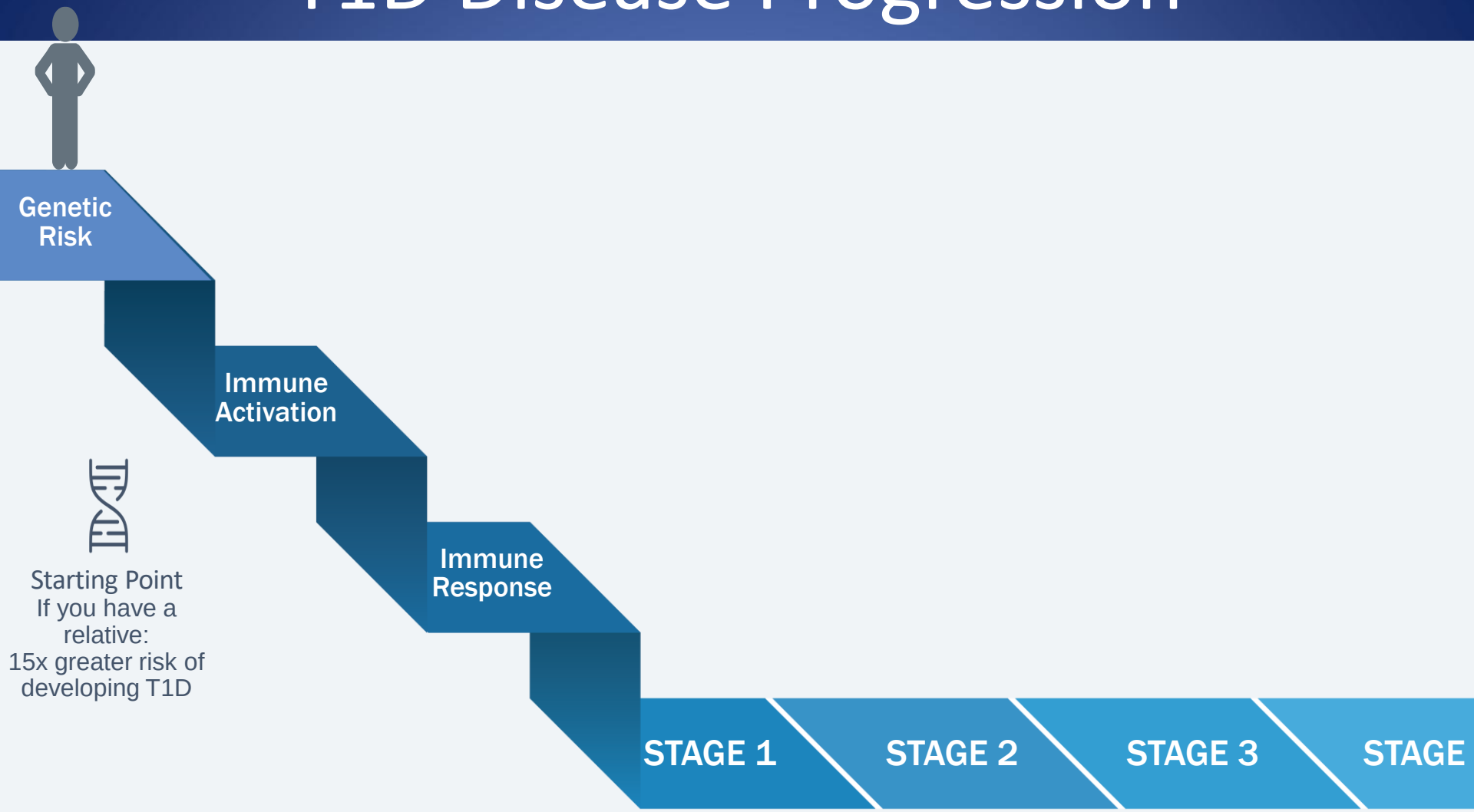
Eisenbarth Model of T1D



T1D Disease Progression



T1D Disease Progression



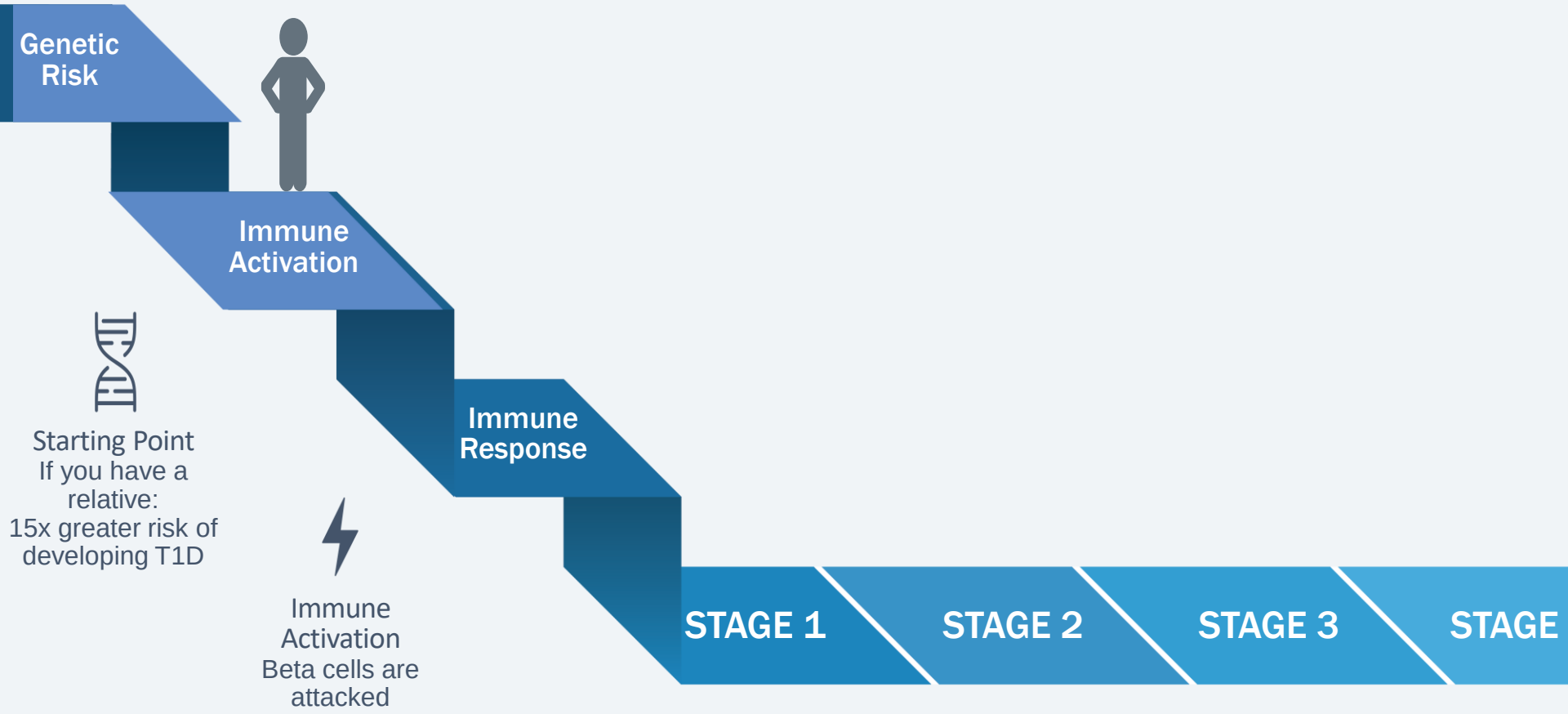
T1D Disease Progression

Starting Point
Genetic Risk

The path to T1D starts here

- Everyone who is diagnosed with T1D has the gene(s) associated with T1D
  - General population risk is 1 in 300
- Family members are at 15x greater risk to develop T1D
  - Relative risk is 1 in 20

T1D Disease Progression



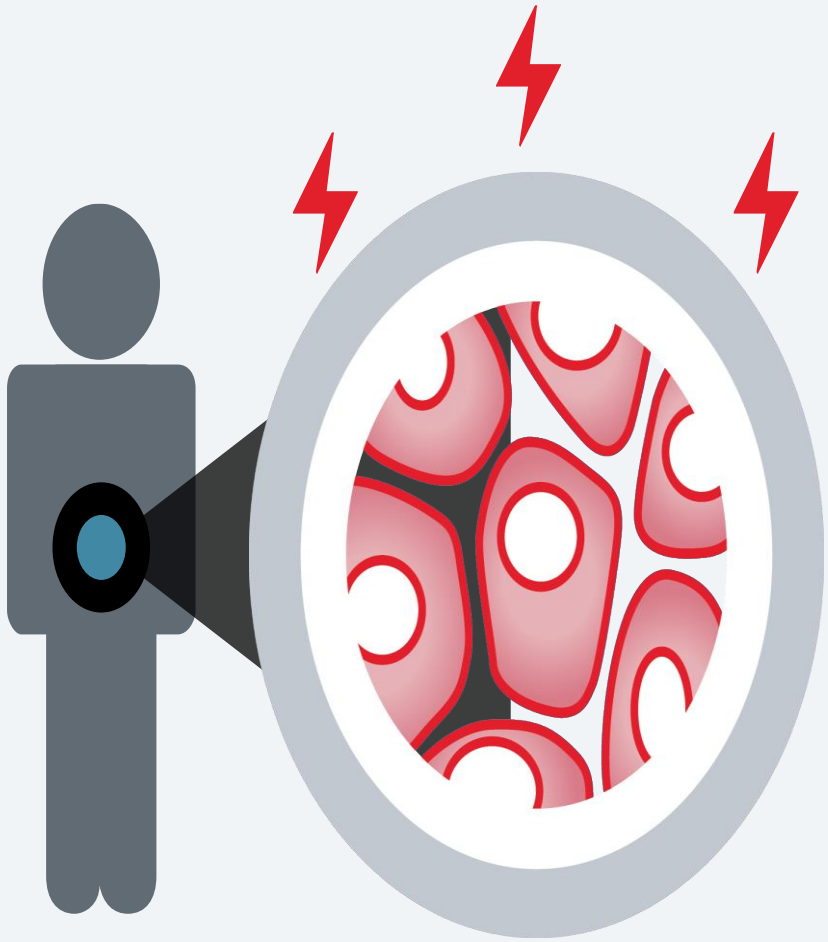
T1D Disease Progression

Immune system is activated

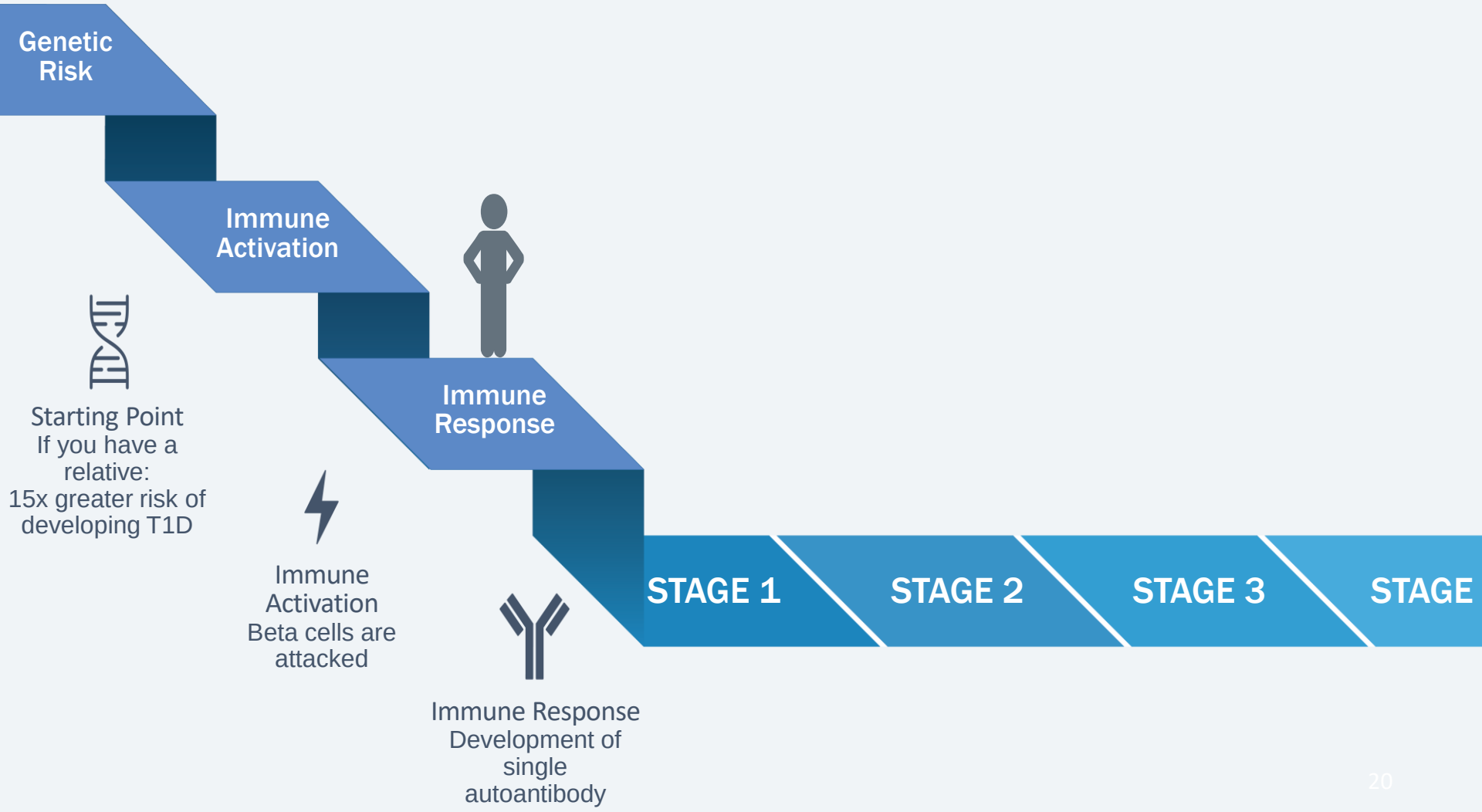
Immune Activation

Immune system attacks beta cells

- Likely a common event
- Research taking place to identify the possible “event” or combination of “events”



T1D Disease Progression



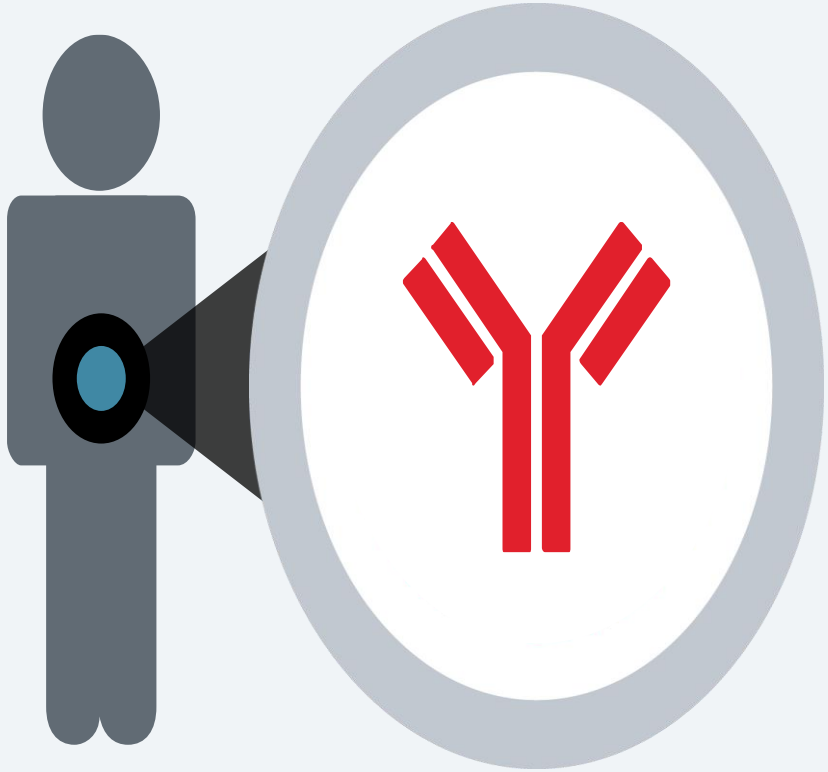
T1D Disease Progression

Development of single autoantibody

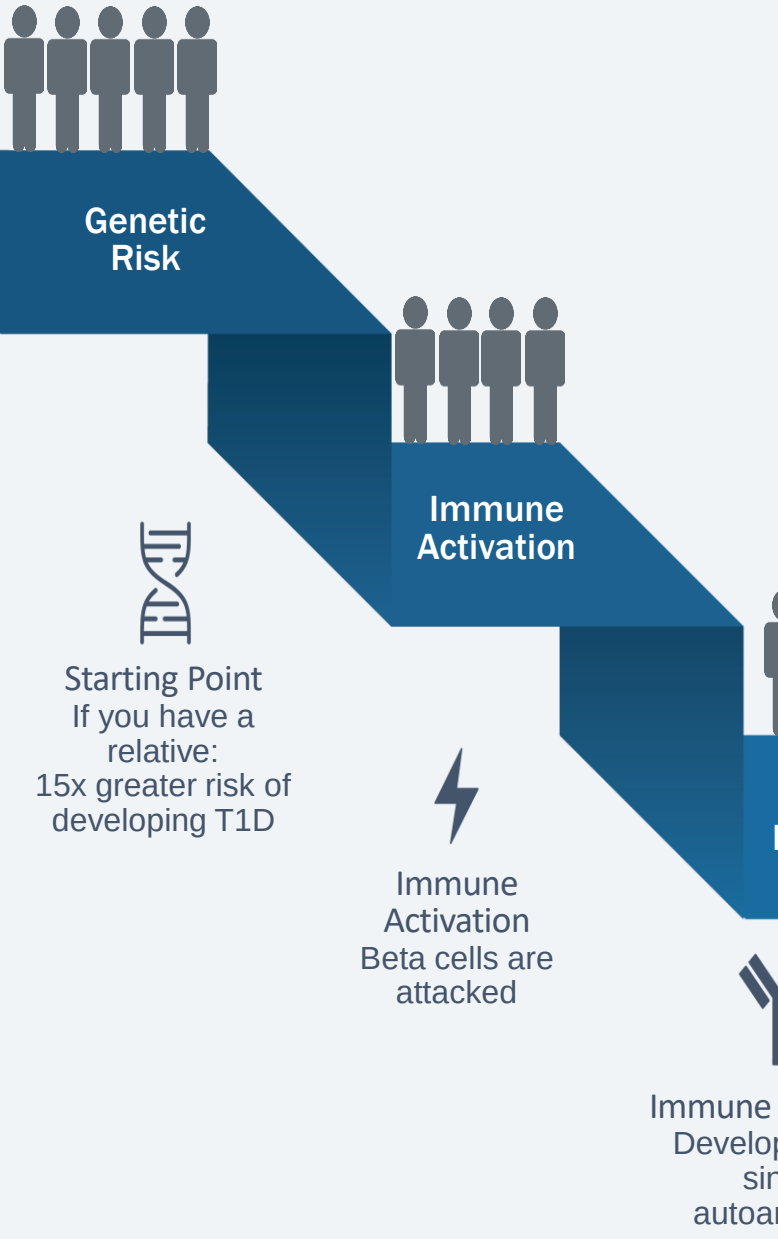
Immune Response

1 autoantibody

- Immune system responds to beta cells being attacked
- Results in the development of autoantibodies
- Autoantibodies are a “visible” signal that the immune system is activated



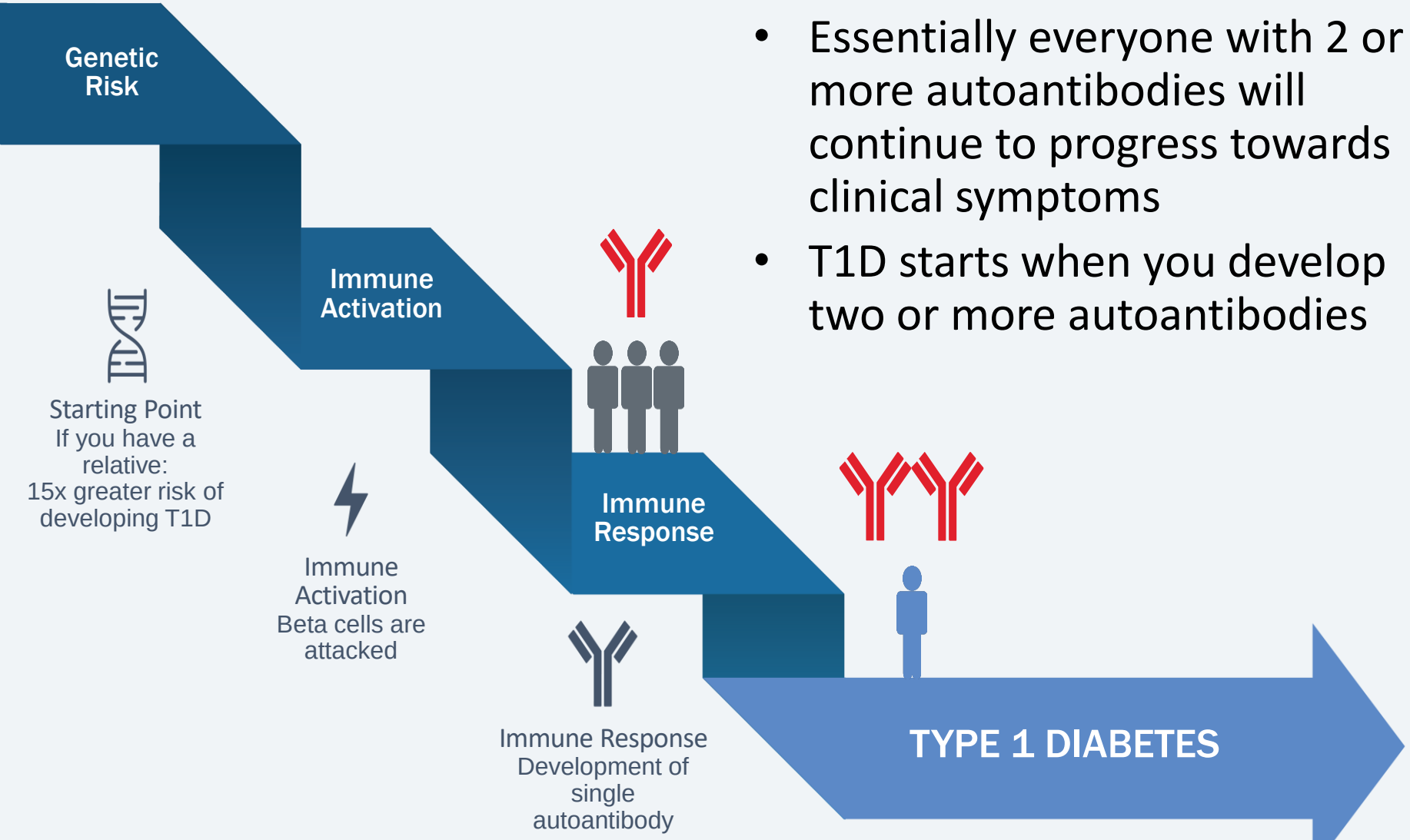
T1D Disease Progression



Progression by Population:

- Everyone who goes onto develop T1D has a genetic risk
- Immune system will be activated in some of those people
- Even fewer will go on to develop an autoantibody

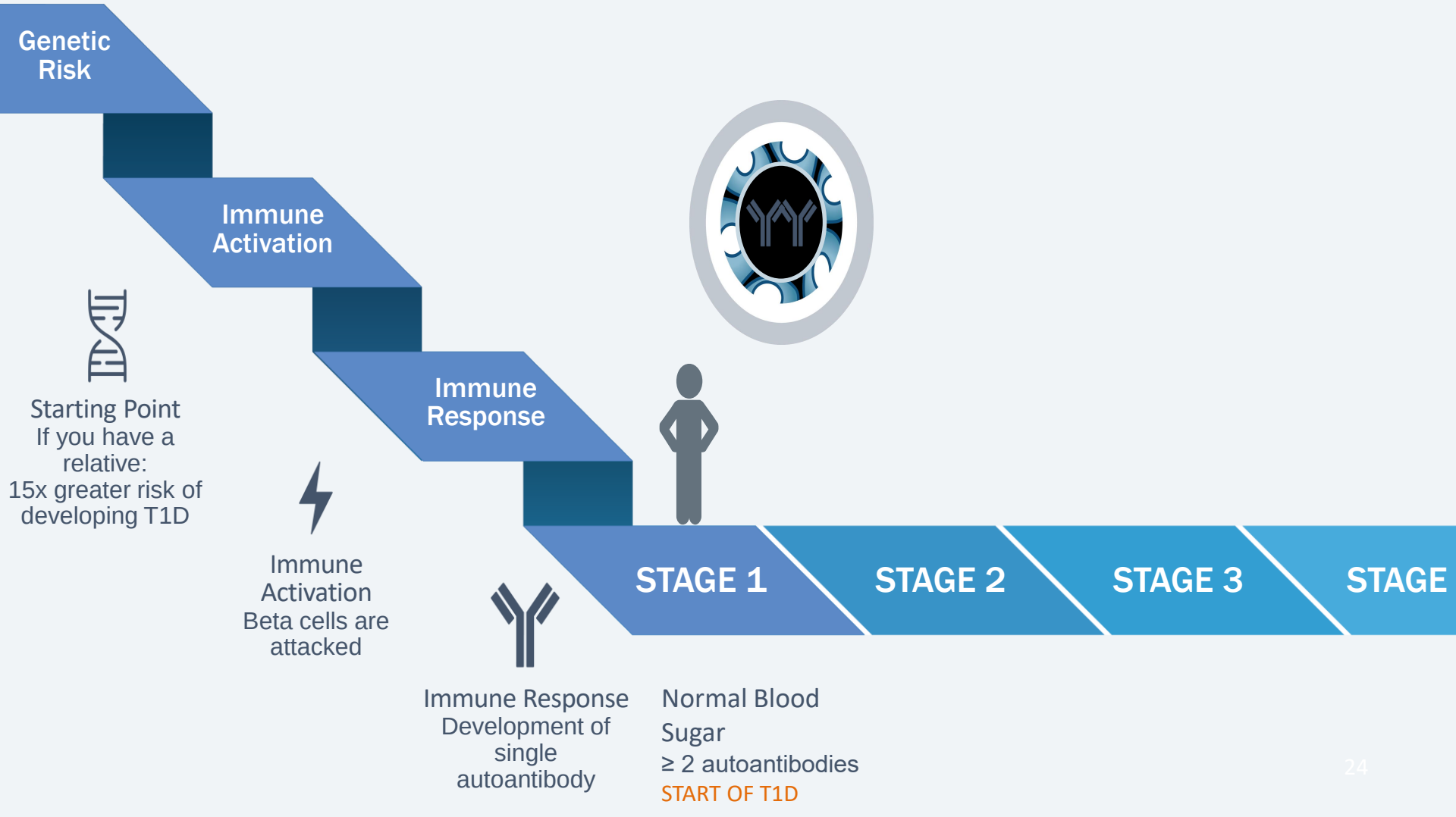
T1D Disease Progression



Progression by Population:

- Essentially everyone with 2 or more autoantibodies will continue to progress towards clinical symptoms
- T1D starts when you develop two or more autoantibodies

T1D Disease Progression

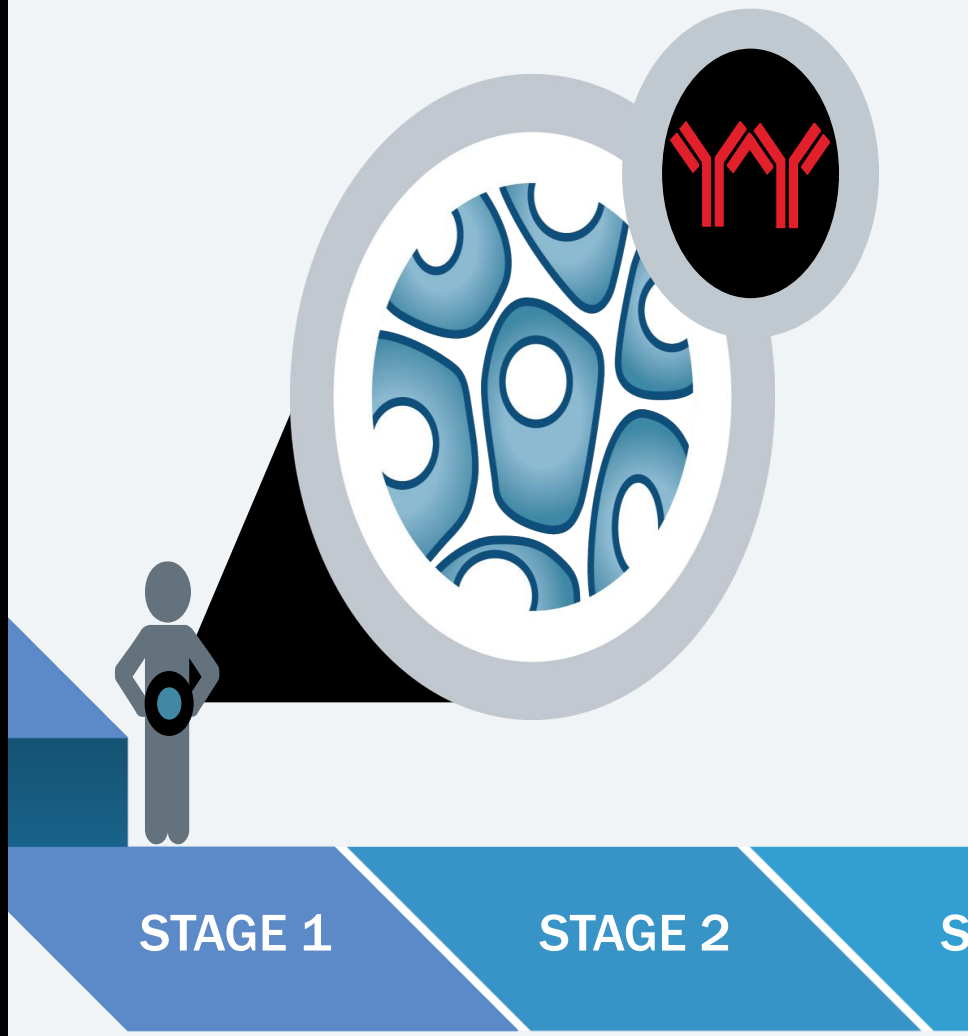


T1D Disease Progression

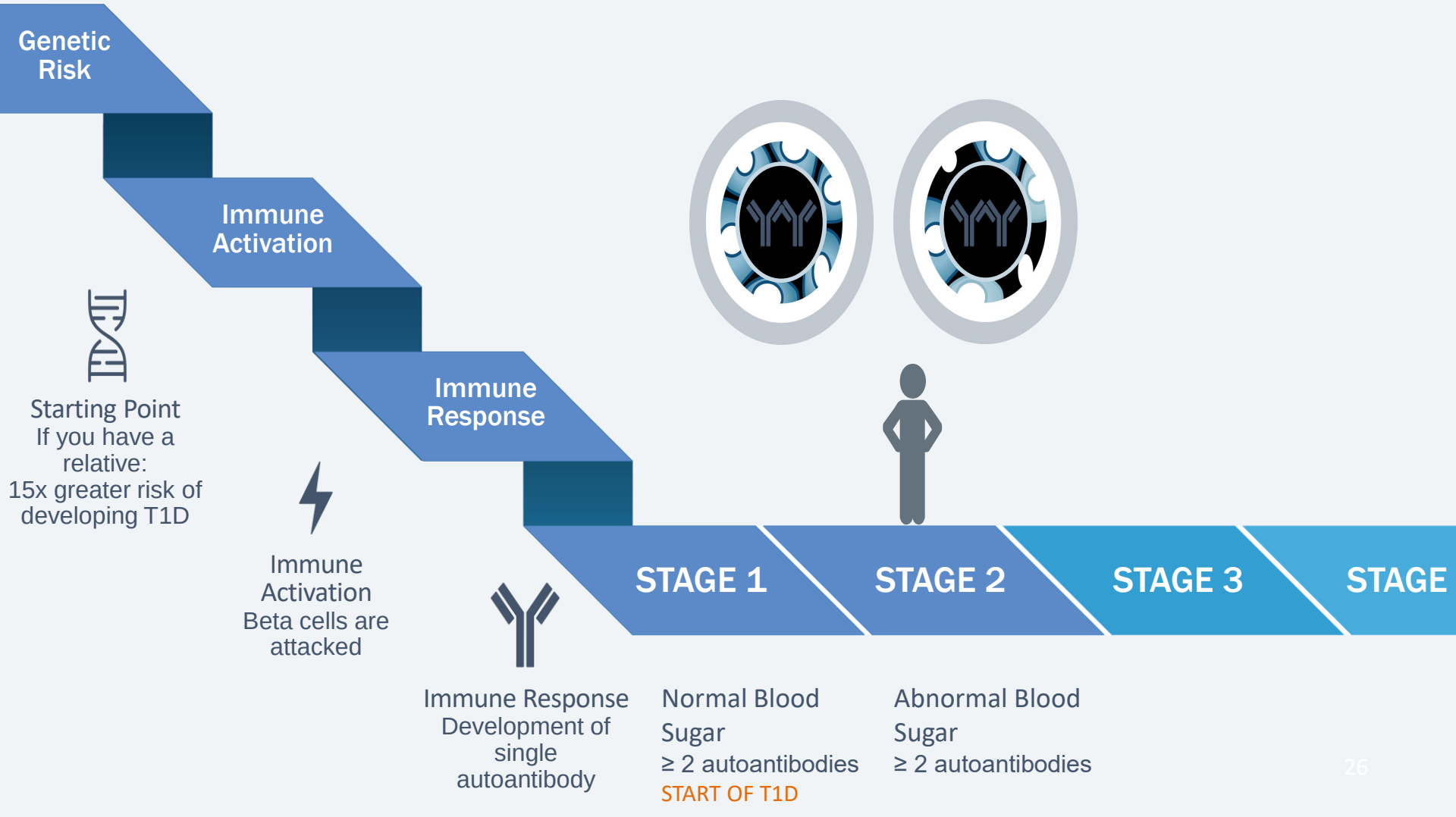
Stage 1 T1D
Normal Blood Sugar

≥ 2 autoantibodies

- START of T1D
- Two or more autoantibodies
- Normal blood sugar
- Lots of beta cells that are able to maintain blood sugar
- No symptoms



T1D Disease Progression

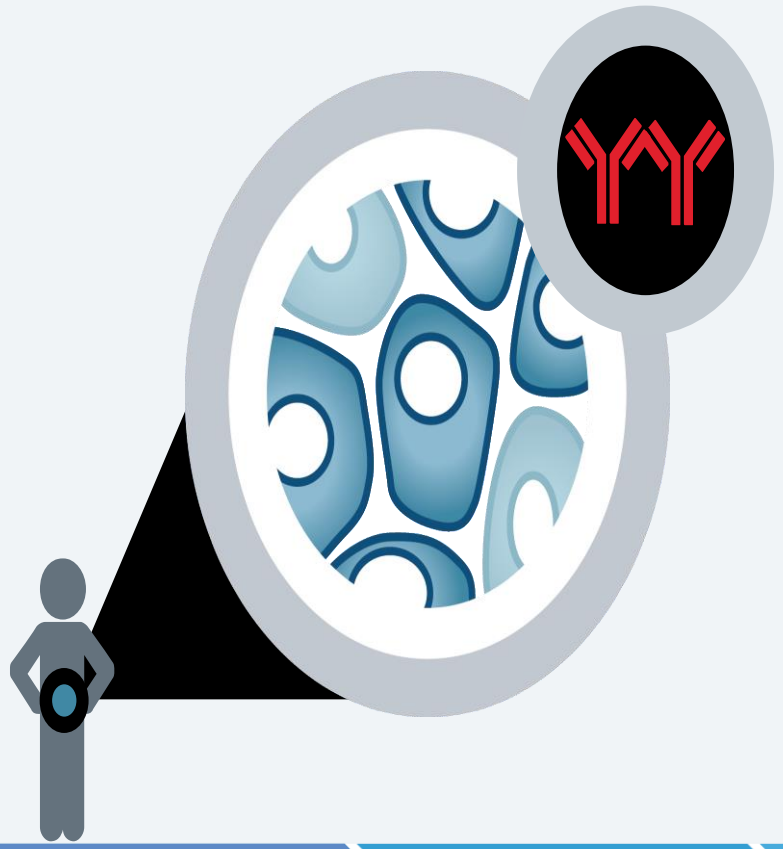


T1D Disease Progression

Stage 2 T1D
Abnormal Blood Sugar

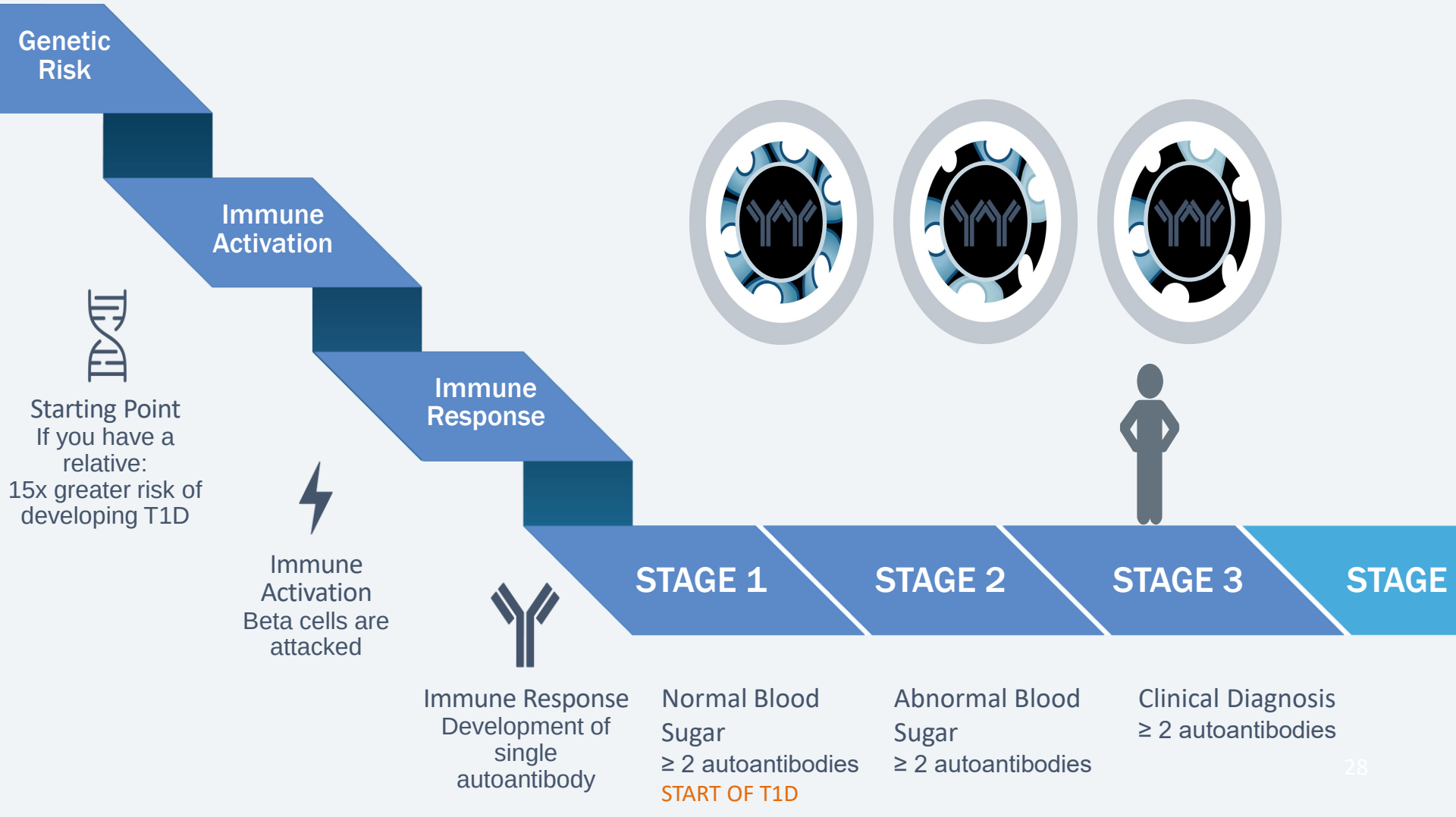
≥ 2 autoantibodies

- Two or more autoantibodies
- Fewer beta cells, but not enough to keep blood sugar normal
- No symptoms



STAGE 1 | STAGE 2 | STAGE 3

T1D Disease Progression



T1D Disease Progression

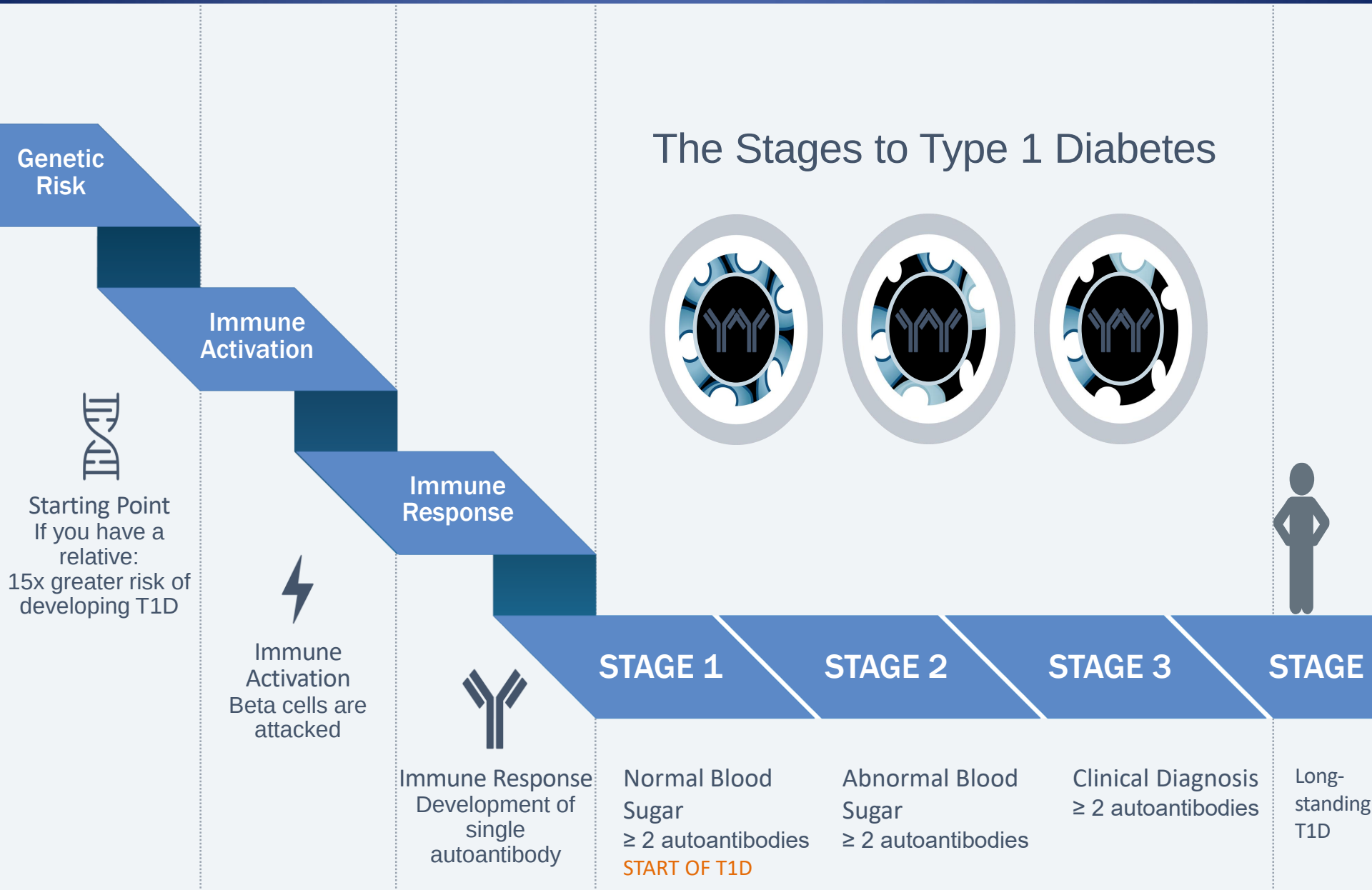
Stage 3 T1D
Clinical Diagnosis

≥ 2 autoantibodies

- Marked by clinical diagnosis (Dx)
- Formerly known as “start of T1D”
- Even fewer beta cells
- Symptoms of high blood sugar

STAGE 1 STAGE 2 STAGE 3 STAGE 4

T1D Disease Progression

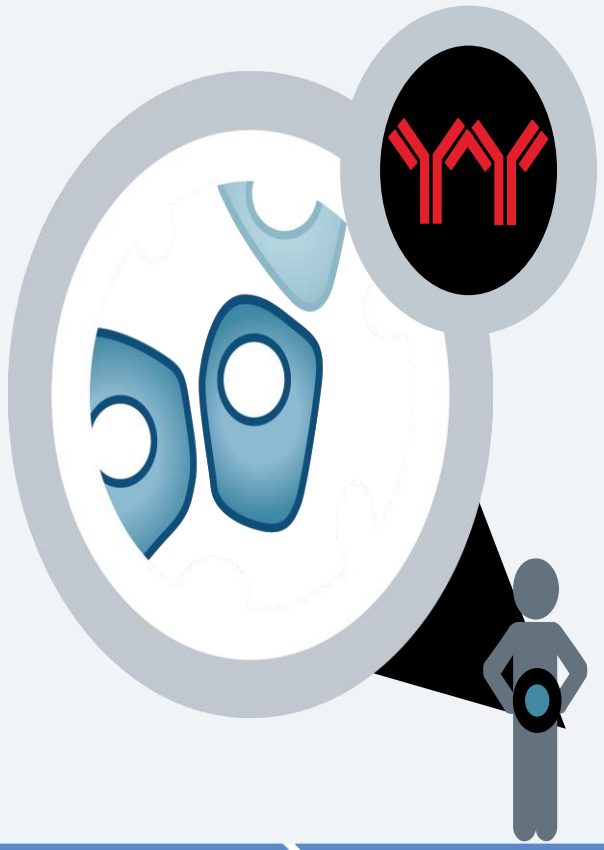


T1D Disease Progression

Stage 4 T1D
Long-Standing T1D

Post diagnosis

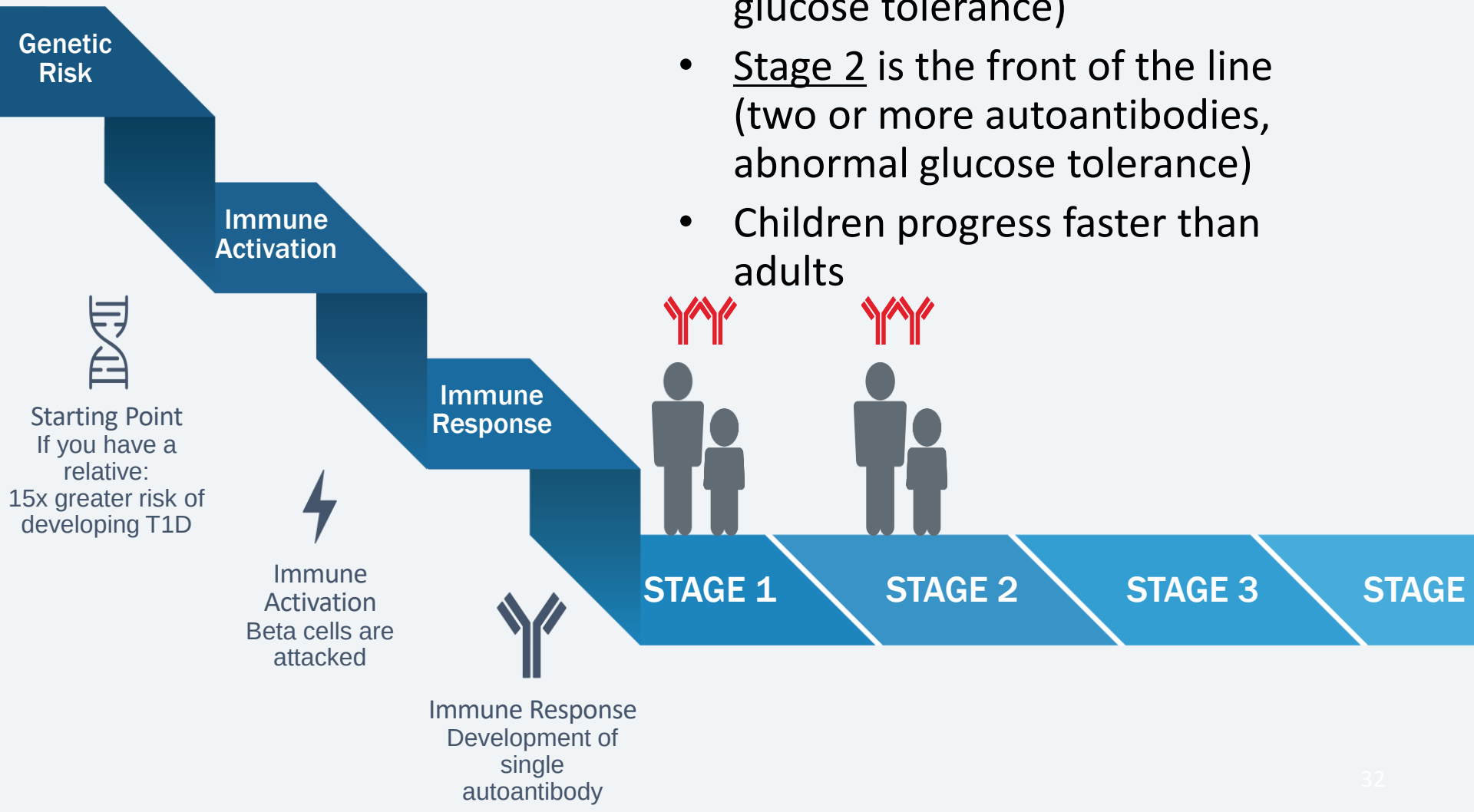
- Continued loss of beta cells over time
- Research outside of TrialNet is working to replace or replenish beta cells



STAGE 2 STAGE 3 STAGE 4

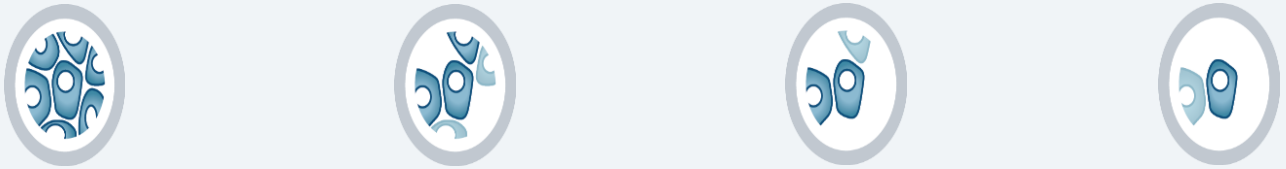
T1D Disease Progression

- Stage 1 is the back of the line (two or more autoantibodies, normal glucose tolerance)
- Stage 2 is the front of the line (two or more autoantibodies, abnormal glucose tolerance)
- Children progress faster than adults



T1D Disease Progression

The impact of AGE on disease progression & beta cell decline



	STAGE 1 (Start of T1D) ≥ 2 autoantibodies	STAGE 2 ≥ 2 autoantibodies	STAGE 3 (Clinical Dx) ≥ 2 autoantibodies	STAGE 4 Long-standing T1D
Age <5				
Age 5-9				
Age 10-14				
Age 15-19				
Age ≥ 20				

T1D Disease Progression

SUMMARY POINTS

1. Type 1 diabetes starts with two or more autoantibodies
2. There are three defined stages:
   - Stage 1: Presence of 2 or more autoantibodies with normal blood sugar
   - Stage 2: Presence of 2 or more autoantibodies with abnormal blood sugar
   - Stage 3: Clinical diagnosis (Dx) of type 1 diabetes
3. Age matters!
   1. Time from 2 or more autoantibodies to Dx is faster the younger you are
   2. Beta-cell decline is also faster the younger you are and continues through stage 4

Diagnosis of Type 1 Diabetes (T1D)

- Usually characterized by insulin deficiency and dependency
  - Document levels of insulin and C-peptide
- Test for autoantibodies
  - Insulin
  - Glutamic acid decarboxylase
  - Pancreatic islet β cells (tyrosine phosphatase IA-2)
  - Zinc transporter (ZnT8)
- May occur in overweight or obese as well as lean individuals
- May occur in adults as well as children

Insulin Era: 1930-1970

Long-term Complications

Visual impairment (legal)	14%	30%
Blindness (total)	16%	
Renal failure	35%	
Stroke	10%	
Amputation	12%	
Myocardial infarction	25%	

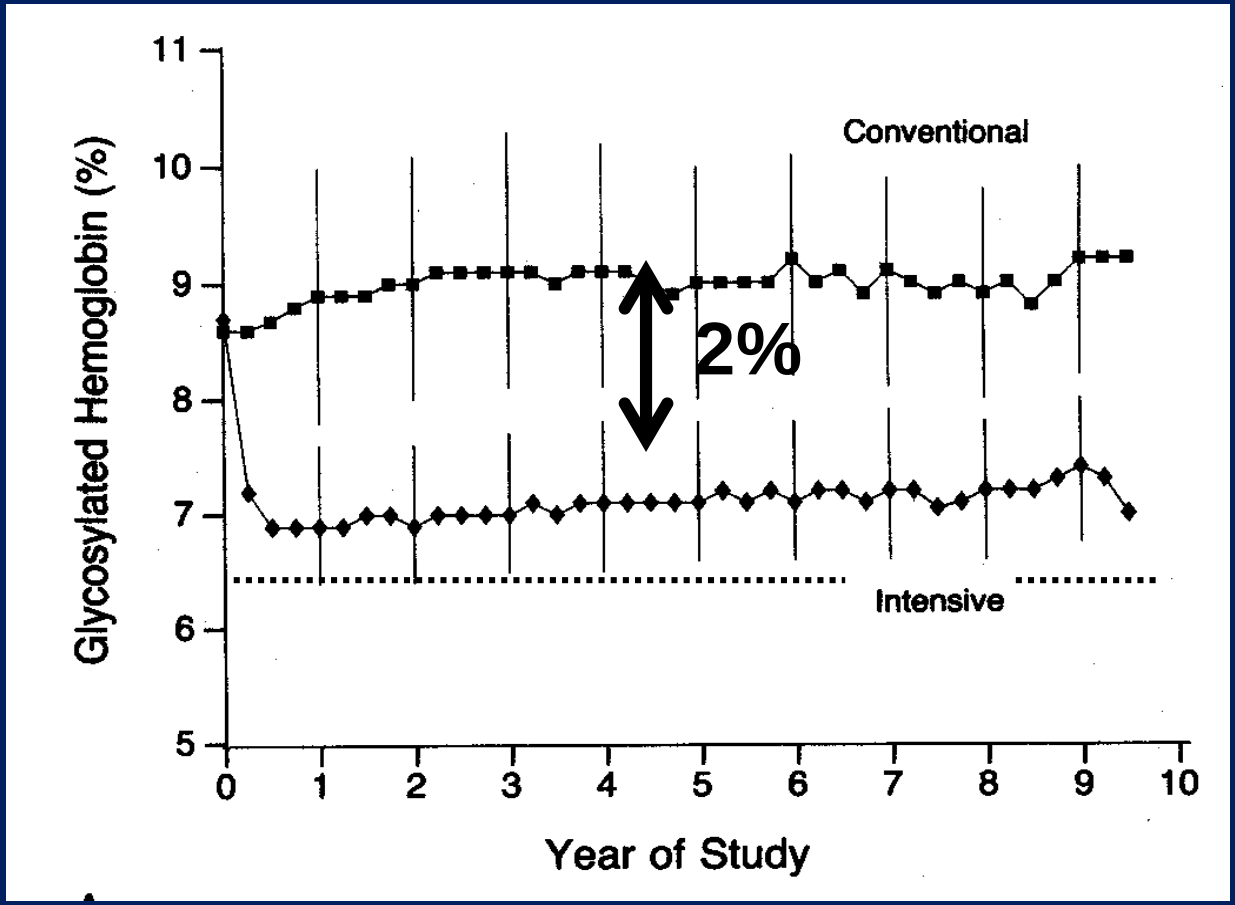
LIFE SPAN REDUCED BY ~ 15 YEARS

DCCT

Metabolic Results

Intensive

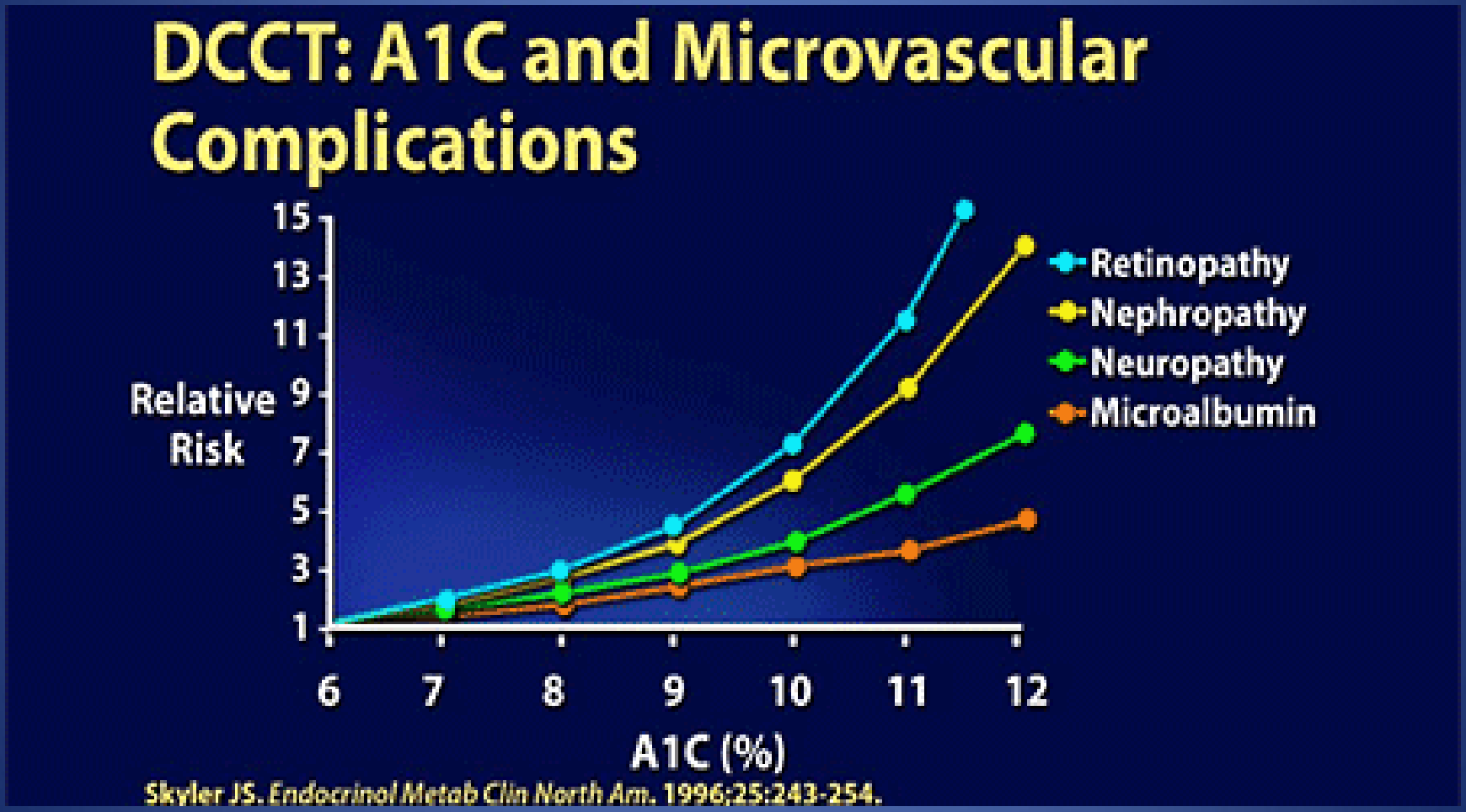
- ≥3 daily injections or CSII- no analogs
- ≥4 SMBG
- Pre-meal BG 70-120 mg/dl (3.9-6.7 mmol/L)
- Post-meal <180 (<10 mmol/L)
- HbA1c <6.05%



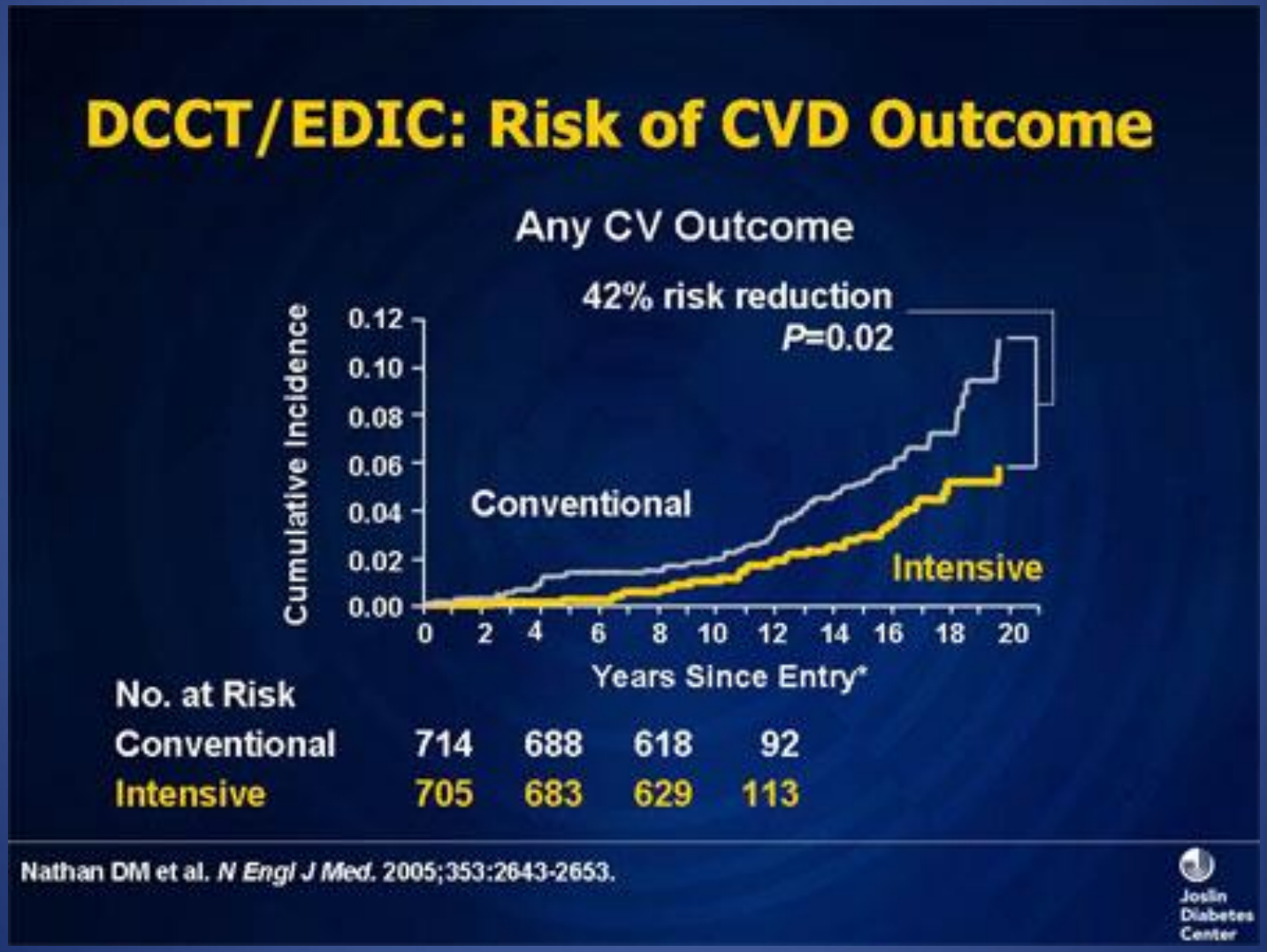
N Engl J Med 1993;342:381

DCCT
DIABETES CONTROL & COMPLICATIONS TRIAL

T1D Landmark Study: DCCT

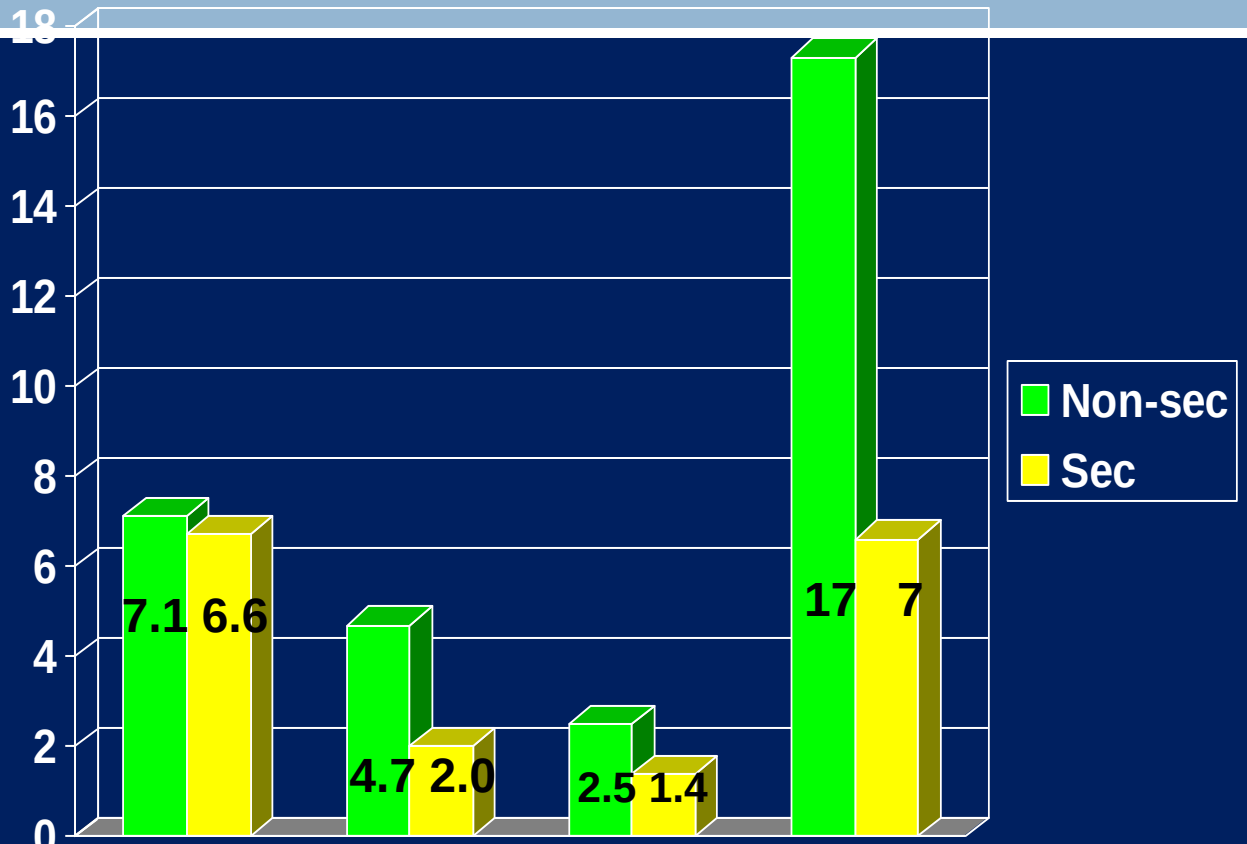


Glucose Control in Cardiovascular Disease Prevention in T1D



Effects of Preserved C-Peptide

Intensively treated Secretors vs Non-secretors



(per 100 patient-years)

Ann Int Med 1998;128:517-23

DIABETES CONTROL & COMPLICATIONS TRIAL

Prevalence (%) of Severe Outcomes after 30 years of T1D

Complication	DCCT INT 2008	STENO 1978
Blindness*	1	30
Renal failure†	1	35
Amputation@	1	12

*<20/200 either eye
† SeCr ≥ 2, dialysis, or transplantation
@All were of toes except one BKA

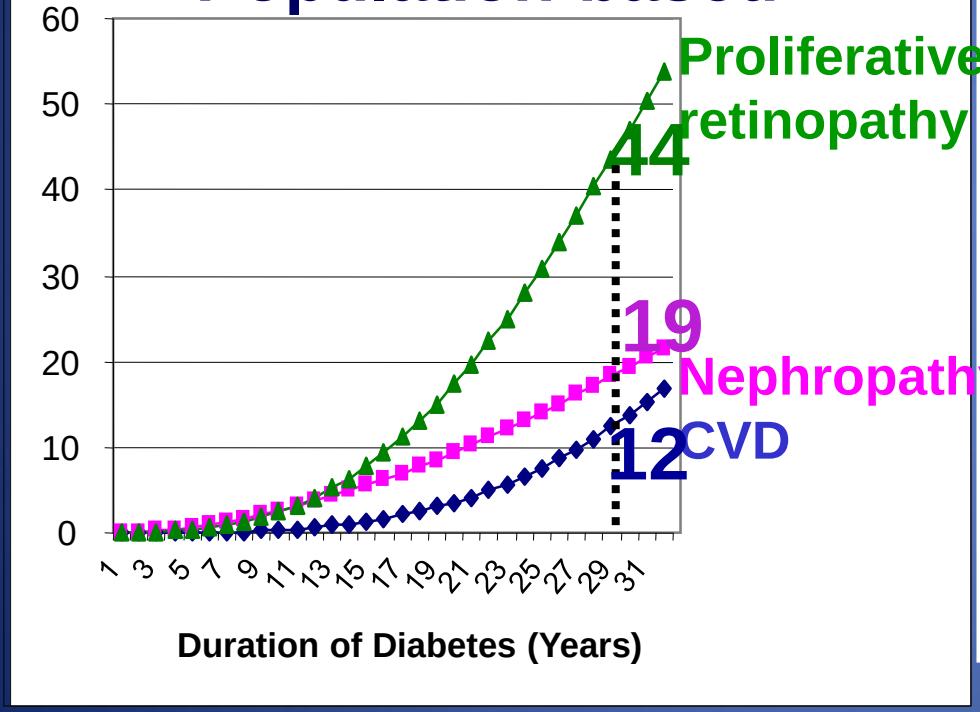
Arch Int Med 2009;169:1307

DCCT/EDIC

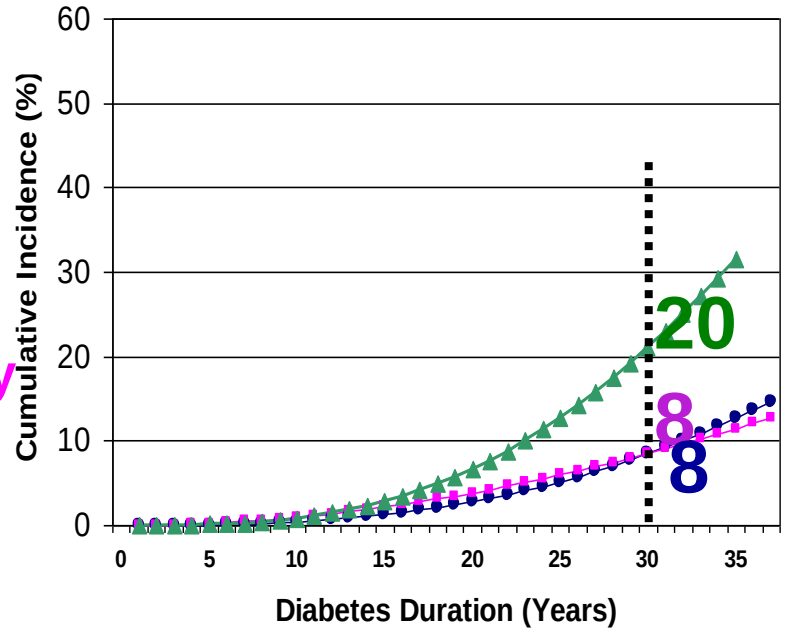
Long-term Outcomes of Type 1 Diabetes

Cumulative Incidence of Advanced Complications After 30 years diabetes duration

Pittsburgh EDC Population-based



DCCT Intensive Therapy



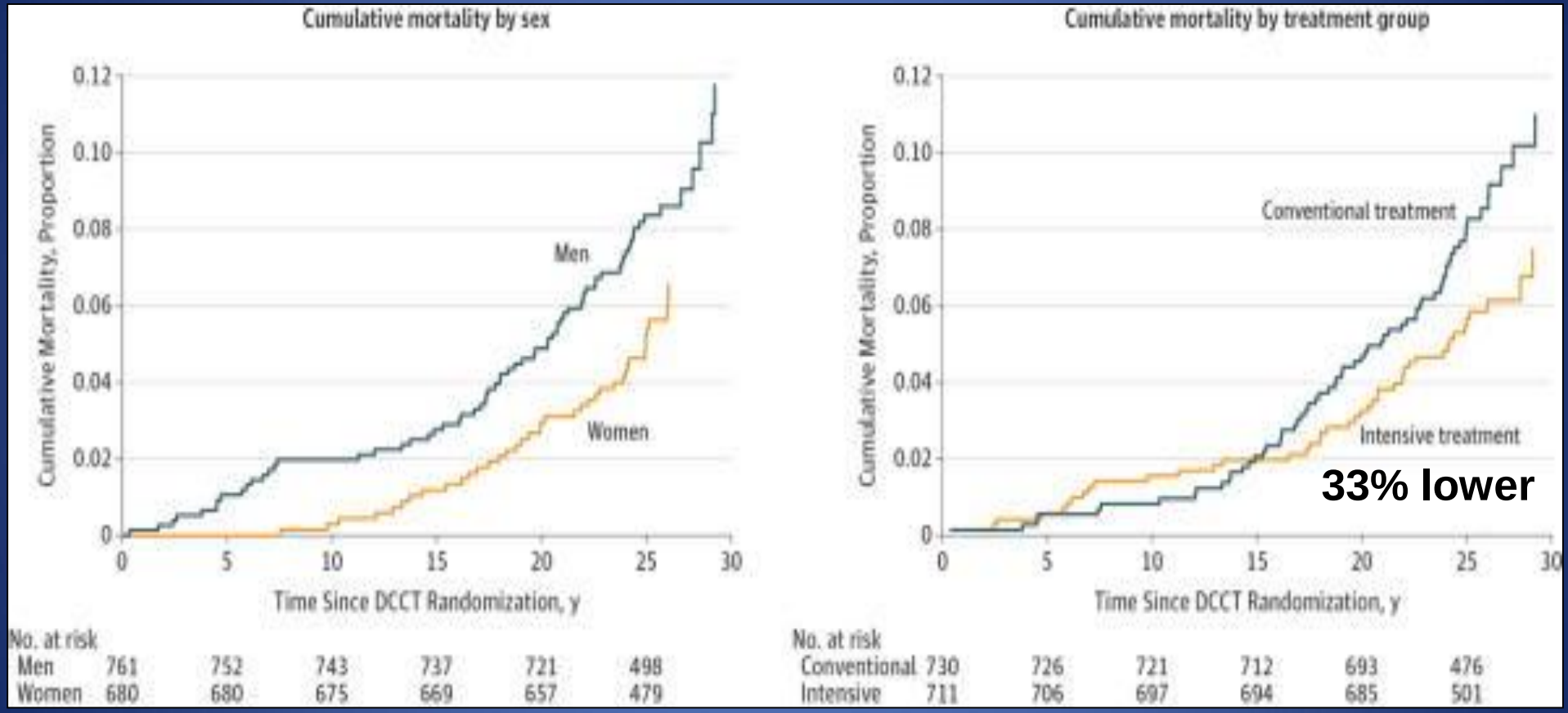
Contemporaneous cohorts ~1980-2008

Arch Int Med 2009;169:1307

DCCT/EDIC

Mortality in T1D

30-year Follow-up of DCCT Cohort



By Sex **By Treatment Group**

Vital status determined in 99.2%

JAMA 2015; 313:45

DCCT/EDIC

Table 1. Target indicators of glycemic control

Level of control	Ideal (non-diabetic)	Optimal	Suboptimal (action suggested)	High risk (action required)
Clinical assessment				
Raised BG	Not raised	No symptoms	Polyuria, polydipsia, and enuresis	Blurred vision, poor weight gain, poor growth, delayed puberty, poor school attendance, skin or genital infections, and signs of vascular complications
Low BG	Not low	Few mild an no severe hypoglycaemias	Episodes of severed hypoglycaemias (unconscious and/or convulsions)	
Biochemical assessment*				
SMBG Values in mmol/l (mg/dl)				
AM fasting or preprandial PG	3.6–5.6 (65–100)	5–8 (90–145)	>8 (>145)	>9 (>162)
Postprandial PG†	4.5–7.0 (80–126)	5–10 (90–180)	10–14 (180–250)	>14 (>250)
Bedtime PG†	4.0–5.6 (80–100)	6.7–10 (120–180)	<6.7 or 10–11 (<120–200)	<4.4 or >11 (<80 or >200)
Nocturnal PG†	3.6–5.6 (65–100)	4.5–9 (80–162)	<4.2 or >9 (<75 or >162)	<4.0 or >11 (<70 or >200)
HBA_{1c} DCCT (%)				
(DCCT standardized)	<6.05	<7.5†	7.5–9.0†	>9.0‡
IFCC (mmol/mol)	< 43	< 58	58-75	>75

Global IDF/ISPAD Guidelines, 2011

Outpatient Glucose Targets for Nonpregnant Adults

Parameter	Treatment Goal
A1C, %	Individualize on the basis of age, comorbidities, duration of disease, and hypoglycemia risk: •In general, ≤6.5 for most* •Closer to normal for healthy •Less stringent for “less healthy”
FPG, mg/dL	<110
2-Hour PPG, mg/dL	<140

*Provided target can be safely achieved.

FPG = fasting plasma glucose; PPG = postprandial glucose.

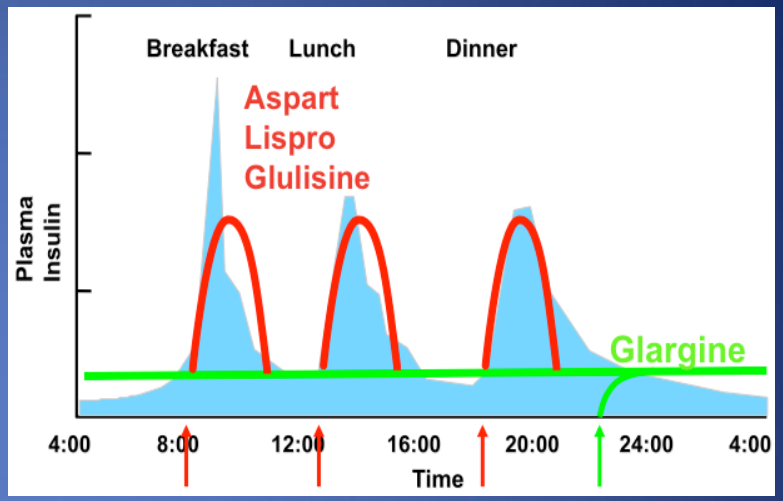
Insulin Regimens

- Insulin is required for survival in T1D
- Physiologic regimens using insulin analogs should be used for most patients

Multiple daily injections (MDI)	Continuous subcutaneous insulin infusion (CSII)
• 1-2 injections basal insulin per day • Prandial insulin injections before each meal	• Insulin pump using rapid acting insulin analog

T1D Management: 2016

- Multi-disciplinary/ technology-driven care
- Insulin: Analogs/ Novel delivery systems
- Glucose monitoring and Continuous glucose monitoring systems (CGMS)
- Enhanced education



Assessment of Diabetic Nephropathy

- Annual assessments
  - Serum creatinine to determine eGFR
  - Urine microalbuminuria
- Begin annual screening
  - 5 years after diagnosis of T1D if diagnosed before age 30 years
  - At diagnosis of T1D in patients diagnosed after age 30 years

AER = albumin excretion rate; eGFR = estimated glomerular filtration rate; T1D = type 1 diabetes; T2D = type 2 diabetes.

Assessment of Diabetic Retinopathy

- Annual dilated examination by ophthalmologist
- Begin assessment 5 years after diagnosis of T1D
- More frequent examinations in:
  - Patients during pregnancy and 1 year postpartum
  - Patients with retinopathy
  - Patients with macular edema

DM = diabetes mellitus; T1D = type 1 diabetes; T2D = type 2 diabetes.

Comprehensive Management of CV Risk

- Manage CV risk factors – EDIC Study
  - Weight management
  - Smoking cessation
  - Optimal glucose, blood pressure, and lipid control
  - Guidelines for use of statins, ACE-I unclear

CV = cardiovascular; CVD = cardiovascular disease.

T1D Registries: US, England/Wales, Germany/Austria

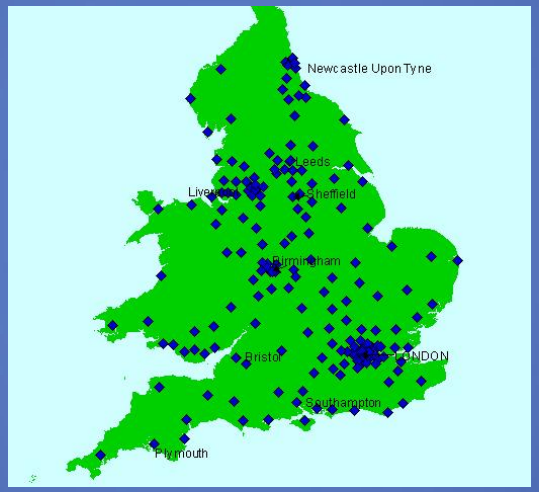
T1D Exchange

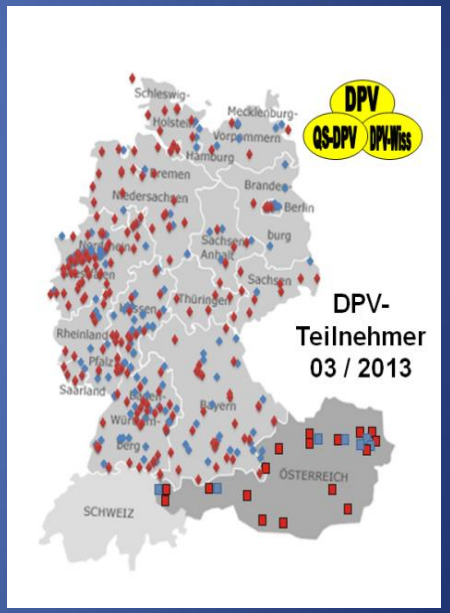
RCPCH Royal College of Paediatrics and Child Health — Leading the way in Children's Health

NPDA National Paediatric Diabetes Audit

HQIP Healthcare Quality Improvement Partnership

DPV QS-DPV DPV-Wiss





- N=25,759
- 71 diabetes centers in US

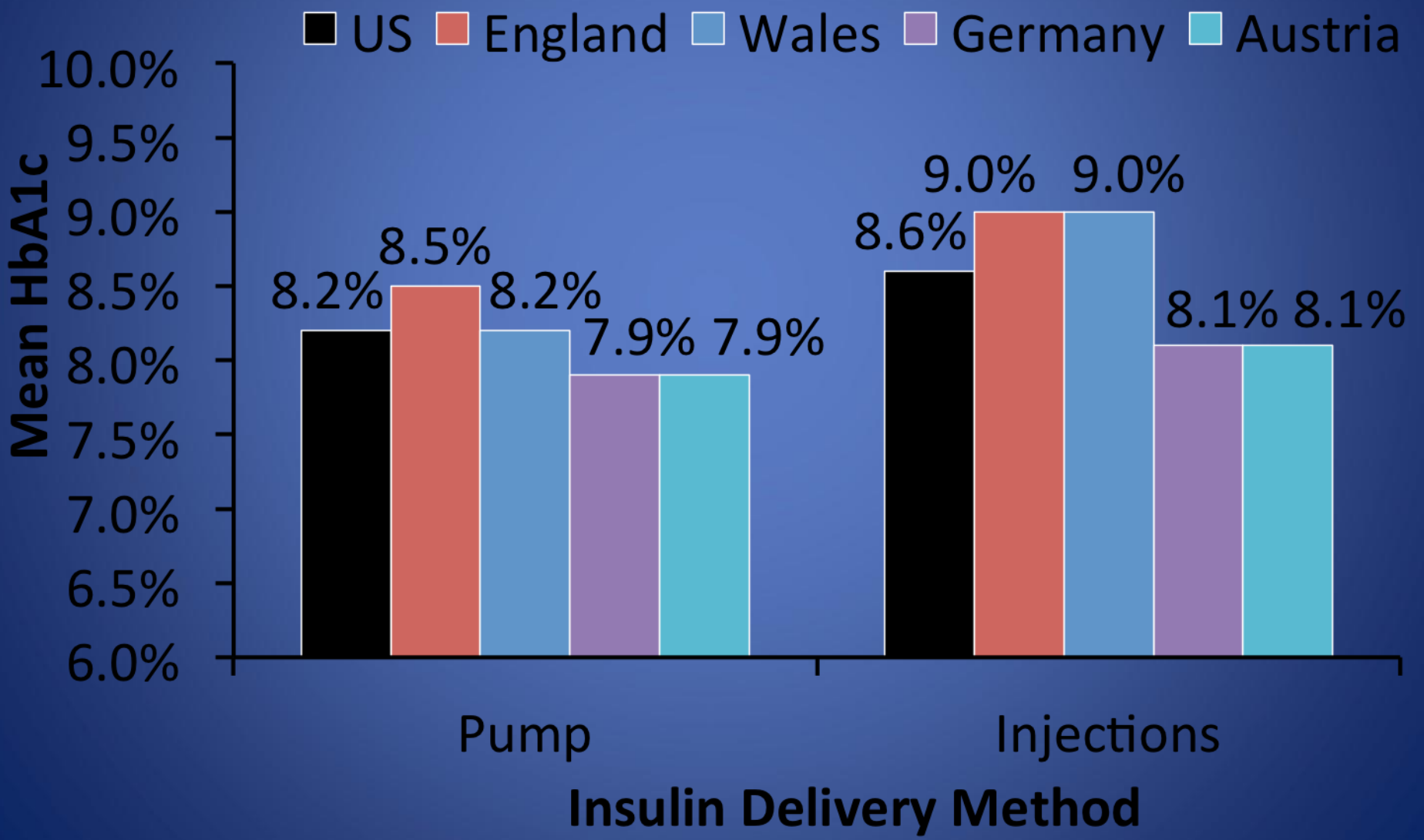
- N=14,539
- 177 paediatric diabetes units in England & Wales

- N=26,262
- 209 pediatric centers in Germany & Austria

Frequency of Pump Use by Age & Registry in Pediatric T1D

	<6 yo	6-<10 yo	10-<14 yo	14-<18 yo	CSII Overall
US n=13,966	33%	44%	50%	49%	47%
England n=13,666	22%	16%	14%	11%	14%
Wales n=873	21%	17%	18%	14%	16%
Germany n=24,483	69%	42%	37%	34%	41%
Austria n=1,779	70%	39%	38%	32%	40%

HbA1c by Insulin Method & Registry in Pediatric T1D



T1D in Adults in T1DX

Table 1: Diabetes Duration and Mean HbA1c by Age

	31-<50 yr old (n=3000)		50-<65 yr old (n=1907)		▯ (n=639)	
Diabetes Duration	**n**	**A1c**	**n**	**A1c**	**n**	**A1c**
<20 yrs	1206	7.6%	486	7.7%	134	7.4%
20-<40 yrs	1657	7.7%	846	7.7%	238	7.6%
▯40 yrs	137	7.6%	575	7.5%	267	7.3%

Table 2: Complications and Comorbidities by Diabetes Duration

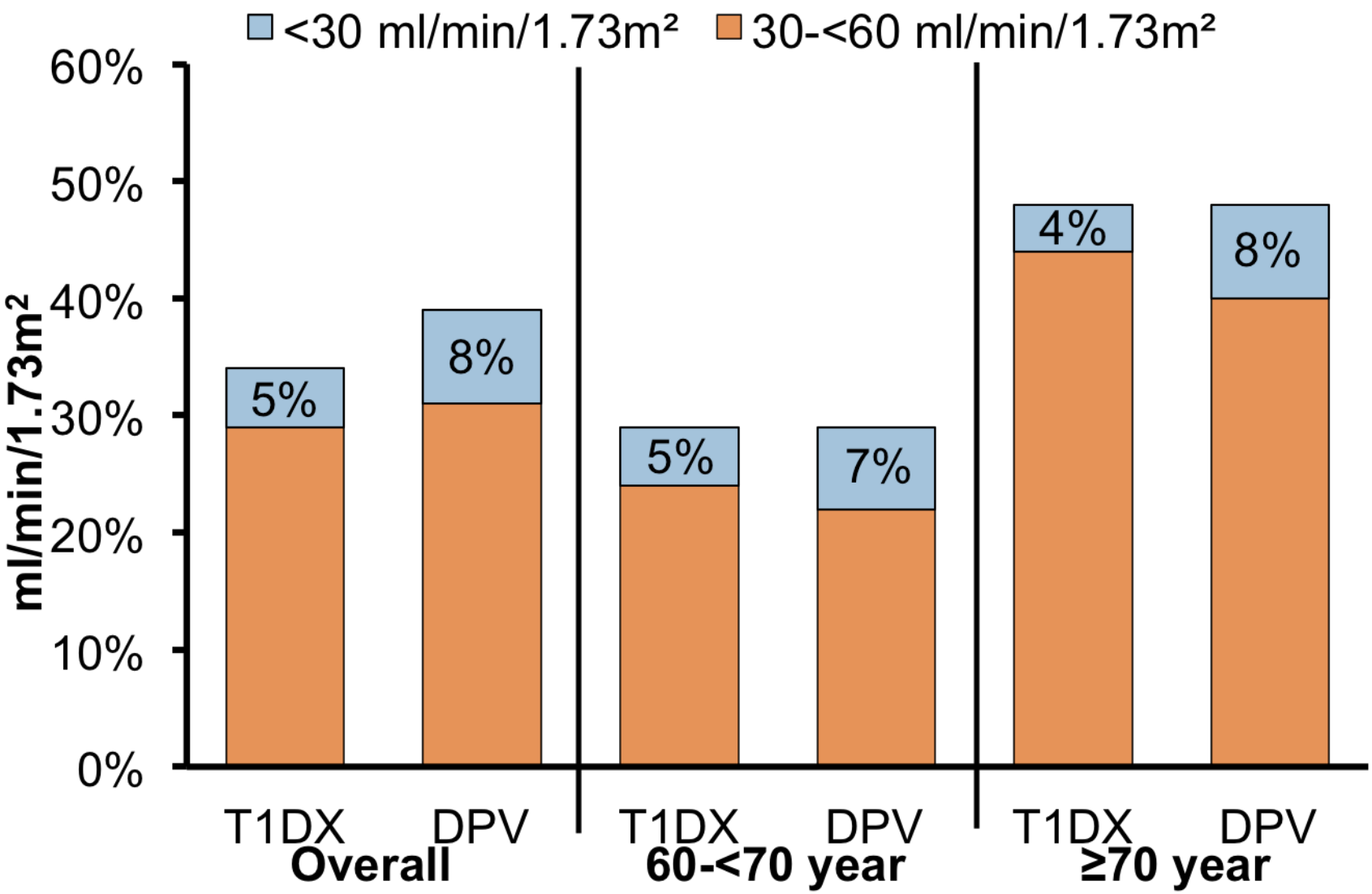
	<20 yrs (n=1826)	20-<40 yrs (n=2741)	▯ (n=979)
Treatment for Retinopathy[a]	3.8%	25%	48%
Nephropathy[b]	5.9%	16%	24%
Neuropathy	7.1%	16%	31%
Myocardial Infarction (MI)	0.9%	1.9%	7.7%
Stroke	0.3%	0.9%	2.8%
Coronary Artery Disease, no MI	2.3%	6.7%	23%

[a]Known laser, injection therapy, or vitrectomy in either eye

[b]Current micro or macroalbuminuria, renal failure (receiving dialysis), or post-kidney transplant

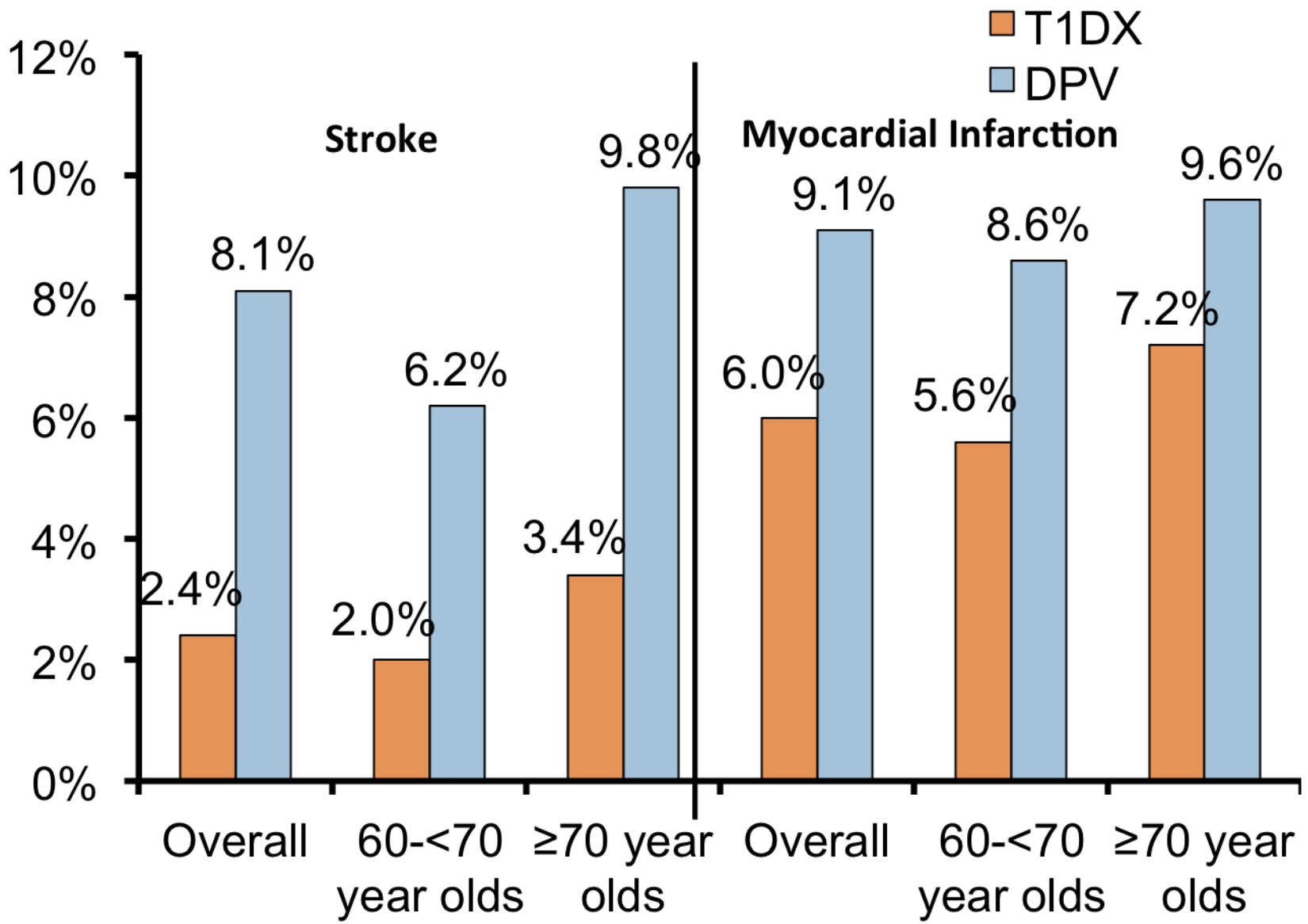
Weinstock, 2012

T1D Adults DPV and T1DX



Weinstock, 2015

T1D Adults DPV and T1DX



Weinstock, 2015

T1D Adults DPV and T1DX

	T1DX N=1285	DPV N=2014	P Value
Age (Yrs.) - *mean*	67	71	<0.001
Male Gender- *%*	48	48	0.99
Diabetes Duration (Yrs.)- *mean*	33	29	<0.001
Mean BMI and % >30 kg/m^2- *mean (%)*	27.3 (25)	27.1 (25)	0.76
Smokers- *%*	6.5	9.7	0.002
HbA1c <7.5%	55	57	0.18
SMBG- *per day*	5.7	4.3	<0.001
Pump Use- *%*	58	18	<0.001
Insulin Dose- *units per kg*	0.54	0.68	<0.001
Systolic Blood Pressure (mmHg)- *mean*	128	136	<0.001*
Diastolic Blood Pressure (mmHg)- *mean*	68	74	<0.001*
Taking ACE-I/ARB- *%*	64	50	<0.001
LDL- cholesterol- *mg/dL*	84	109	<0.001
Taking Statin- *%*	100	40	<0.001
Taking Aspirin- *%*	56	21	<0.001
Depression- *%*	16	8.7	<0.001

Weinstock, 2015

Mortality Benefit from Good T1D Control: Metabolic Memory

- A1Cs converge after DCCT study conclusion but benefit persists
- EDIC Study: Mortality benefit in original intensive group (Orchard, JAMA, 2015)
- Excess mortality largely linked to development of albuminuria and subsequent renal disease and cardiovascular disease
- Mortality not linked to hypoglycemia

T1D "Metabolic Memory"

Mortality Benefit in DCCT:

"After a mean of 27 years' follow-up of patients with T1D, 6.5 years of initial intensive therapy was associated with a modestly lower all-cause mortality compared with conventional therapy." Orchard, 2015

Table 1 : Epidemiology of Diabetes Intervention and Complications (EDIC) study: Key findings

Complication (years of follow up)	% reduction in former intensive treatment group
Retinopathy (10 years EDIC)	
Progression of retinopathy	24
Progression to Proliferative retinopathy	59
Nephropathy (8 years EDIC)	
New microalbuminuria	59
Clinical albuminuria	84
Neuropathy (8 years EDIC)	
Symptoms	51
Signs	43
Cardiovascular disease (17 years DCCT+EDIC)	
Any	42
Non-fatal myocardial infarct, stroke or CVD death	57

CVD = cardiovascular disease;
DCCT = Diabetes Control and Complications Trial

A1C Differs by Minority Group in T1DX

	Age Group							
	1-<13		13-<18		18-<26		□	
	Pump	Injection	Pump	Injection	Pump	Injection	Pump	Injection
Non-Hispanic White	8.0%	8.4%	8.5%	8.9%	8.2%	8.7%	7.6%	7.9%
Non-Hispanic Black	8.5%	9.2%	9.1%	9.9%	9.0%	10.3%	8.0%	8.7%
Hispanic	7.9%	8.3%	8.3%	9.0%	8.3%	9.0%	7.6%	8.3%

*Means are adjusted for SES (household income and insurance), SMBG per day, and T1D duration

Kingensmith, 2012

Pump Use: Differs in Minority Groups in T1DX, DPV and UK T1D Registries

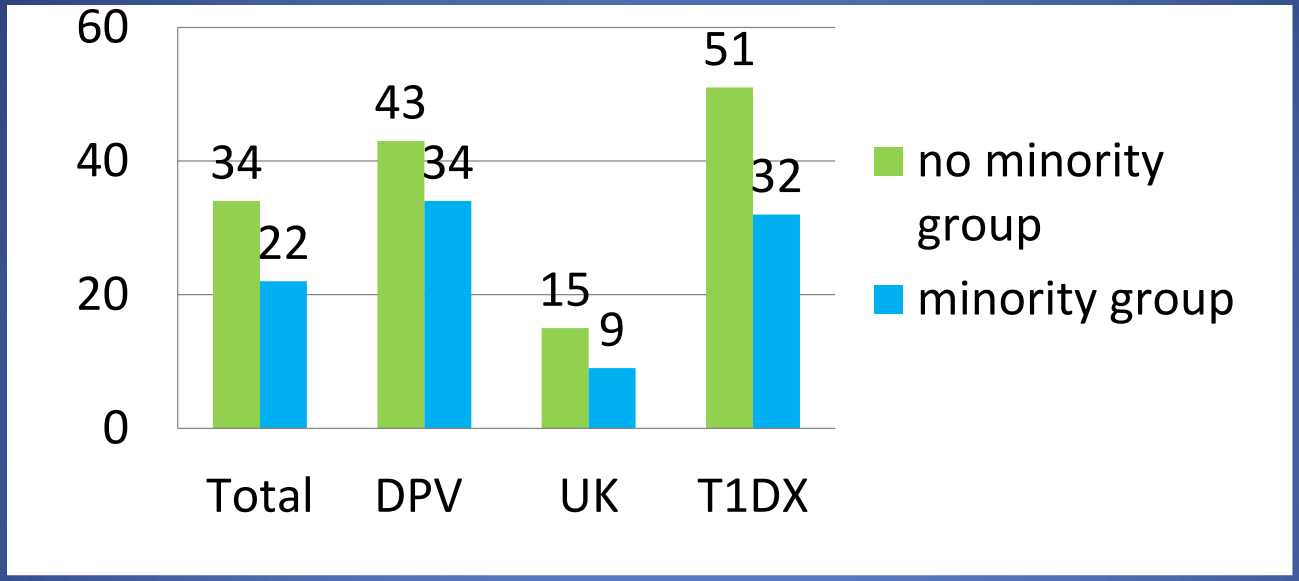
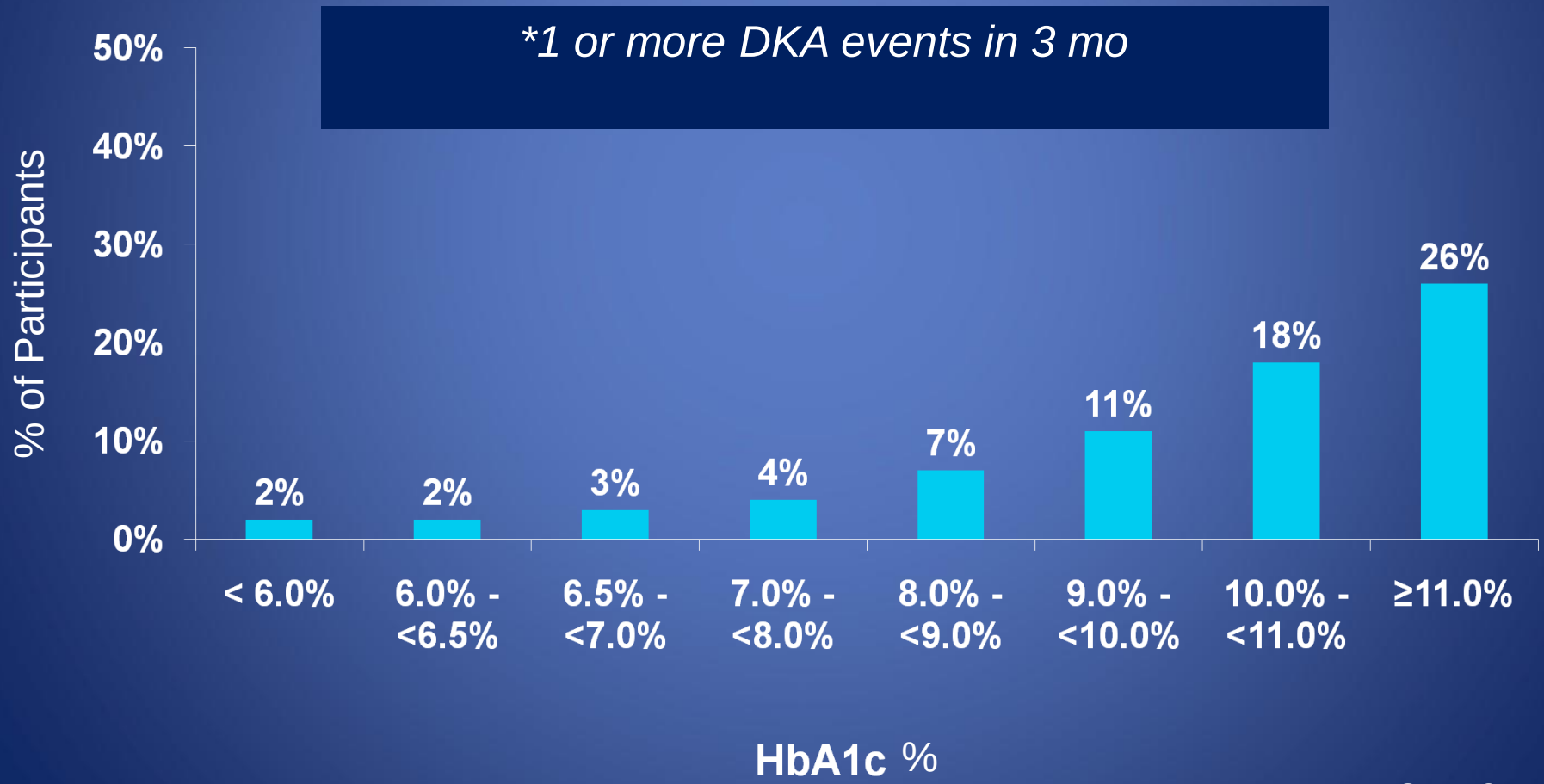


Table 1. Patients characteristics.	DPV	UK	T1DX
n=	26262	14539	13966
% males	52,7	52,6	51,6
age (yrs) mean ± SD	11,5 ± 4,1	12,2 ± 3,6	11,8 ± 3,8
age at onset (yrs) mean ± SD	7,6 ± 4,1	7,4 ± 3,9	6,8 ± 3,9
diabetes duration (yrs) mean ± SD	3,8 ± 3,7	4,8 ± 3,6	4,1 ± 3,7
% minorities	20 ± 0,4	23,8 ± 0,4	22,2 ± 0,4
HbA1c DCCT (rel. %)	8,0 ± 1,6	8,9 ± 1,6	8,3 ±1,4

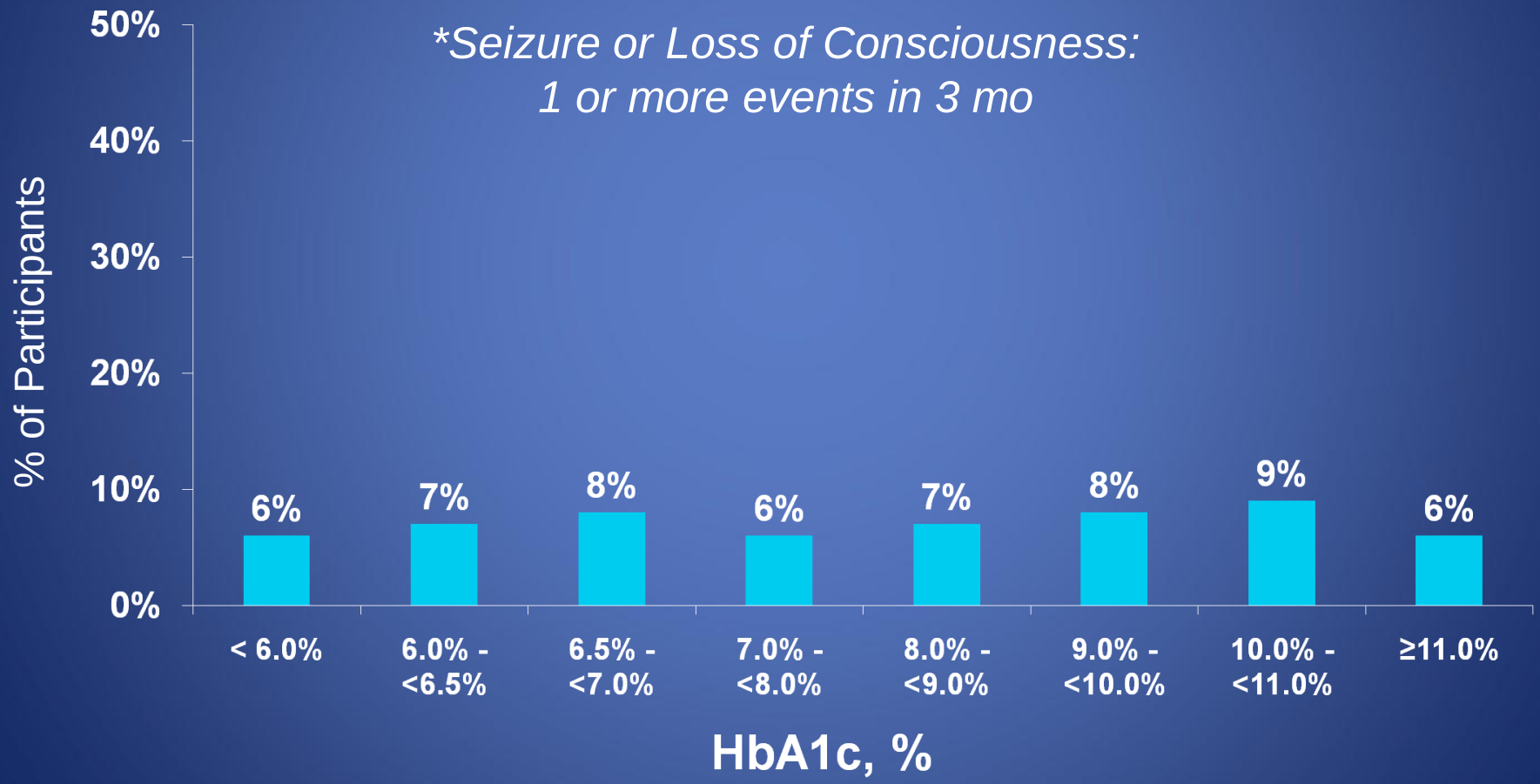
Rami-Merhar 2014

DKA in Past 3 Months in T1DX



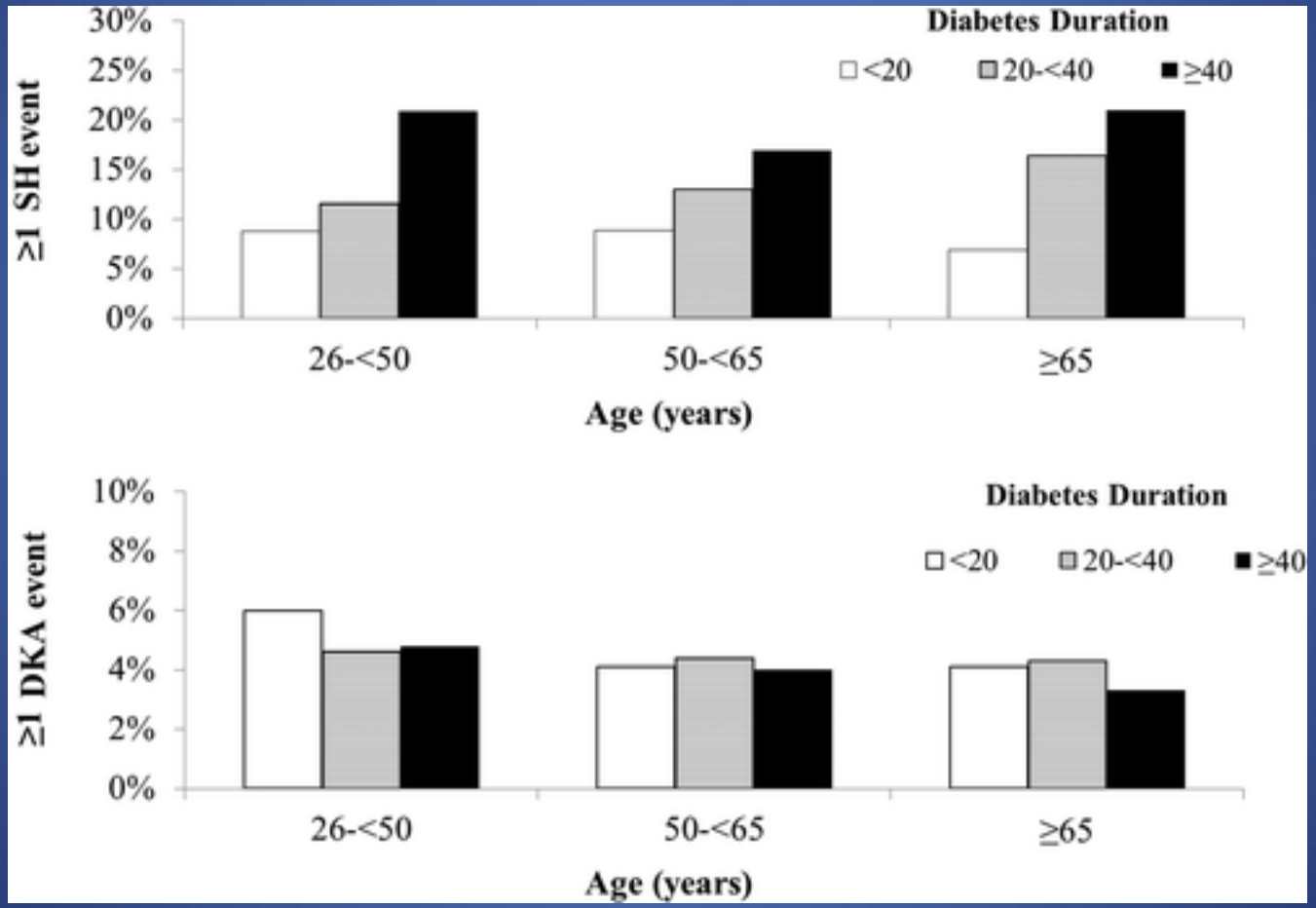
N = 2,756

Hypoglycemia in Past 3 Months in T1DX



N = 2,756

Hypoglycemia in Past 3 Months in Adults in T1DX



Weinstock, JCEM, 2013

Limitation of Therapy: Hypoglycemia

Classification	Blood Glucose Level (mg/dL)	Typical Signs and Symptoms
Mild hypoglycemia	~50-70	• Neurogenic: palpitations, tremor, hunger, sweating, anxiety, paresthesia
Moderate hypoglycemia	~50-70	• Neuroglycopenic: behavioral changes, emotional lability, difficulty thinking, confusion
Severe hypoglycemia	<50*	• Severe confusion, unconsciousness, seizure, coma, death • Requires help from another individual
*Severe hypoglycemia symptoms should be treated regardless of blood glucose level.		

Potential Hypoglycemia Consequences

- Cognitive, psychological changes (eg, confusion, irritability)
- Accidents
- Falls
- Recurrent hypoglycemia and hypoglycemia unawareness
- Refractory diabetes
- Dementia (elderly)
- CV events
  - Cardiac autonomic neuropathy
  - Cardiac ischemia
  - Angina
  - Fatal arrhythmia

Treatment of Hypoglycemia

Hypoglycemia symptoms
(BG <70 mg/dL)

Patient conscious and alert

- Consume glucose-containing foods (fruit juice, soft drink, crackers, milk, glucose tablets); avoid foods also containing fat
- Repeat glucose intake if SMBG result remains low after 15 minutes
- Consume meal or snack after SMBG has returned to normal to avoid recurrence

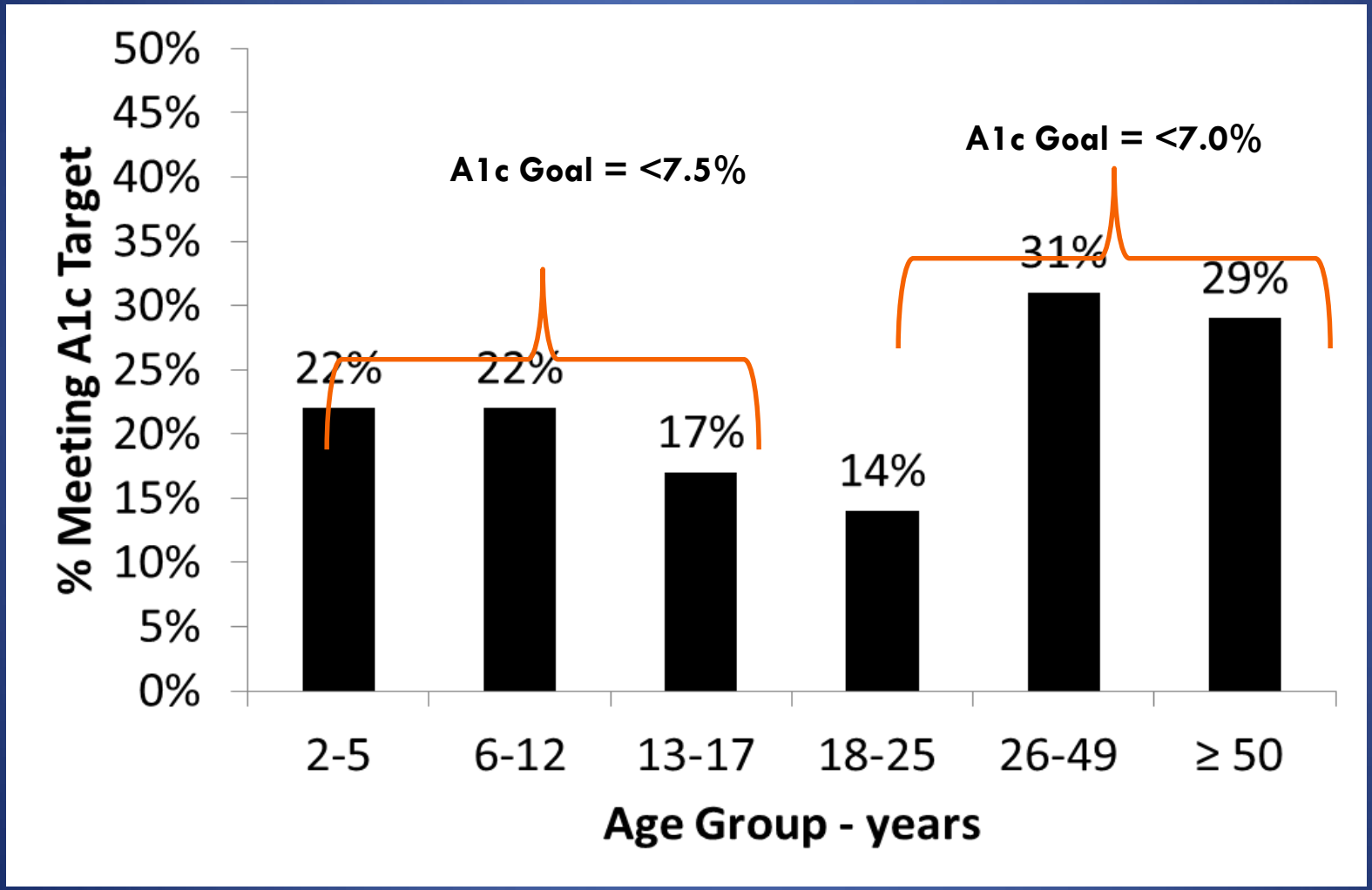
Patient severely confused or unconscious (requires help)

- Glucagon injection, delivered by another person
- Patient should be taken to hospital for evaluation and treatment after any severe episode

PREVENTION IS KEY; ADJUST INSULIN; CONSIDER CGMS

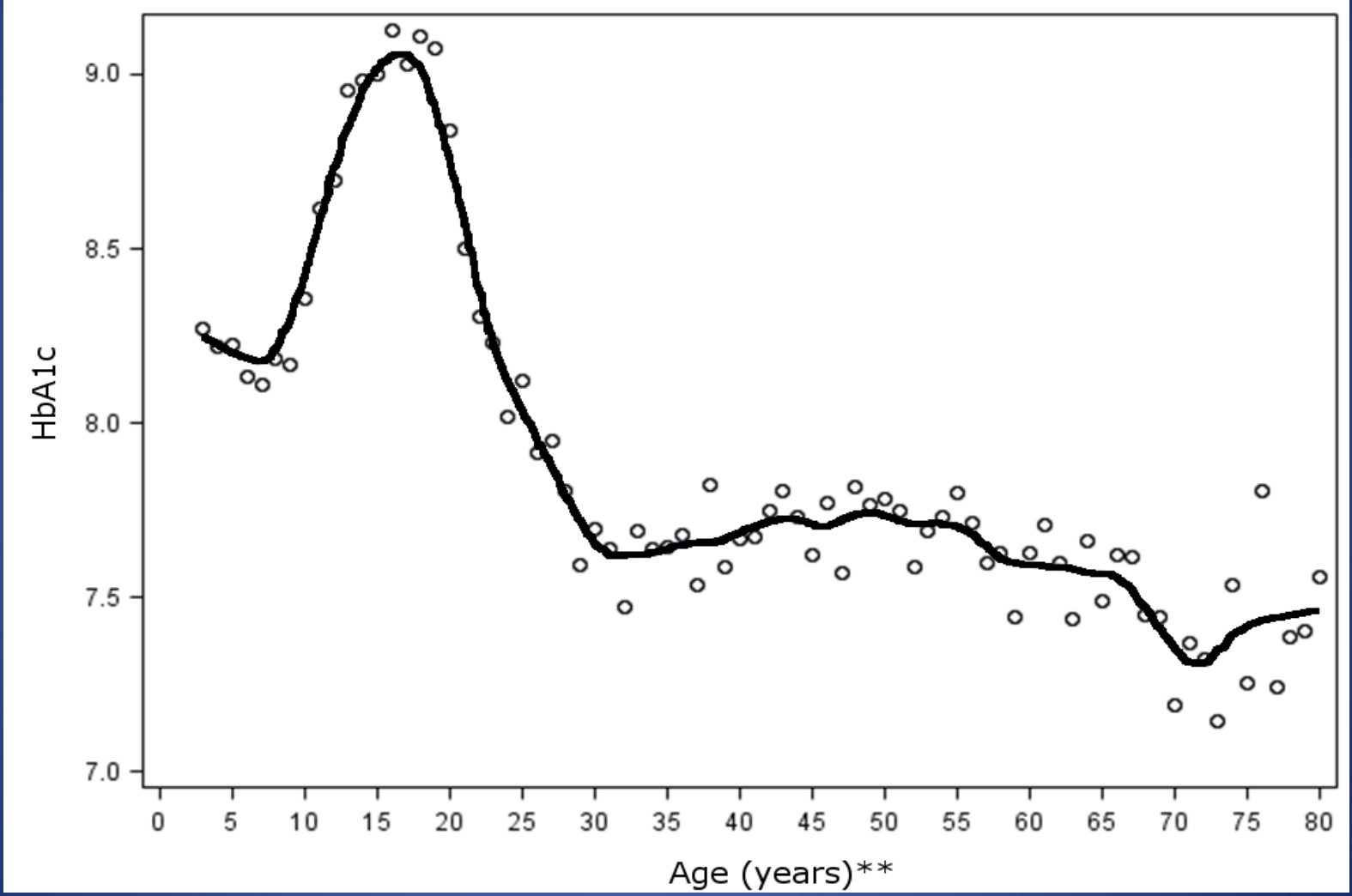
BG = blood glucose; SMBG = self-monitoring of blood glucose.

A1C in T1DX



N = 16,791

A1C by Age in T1D Exchange

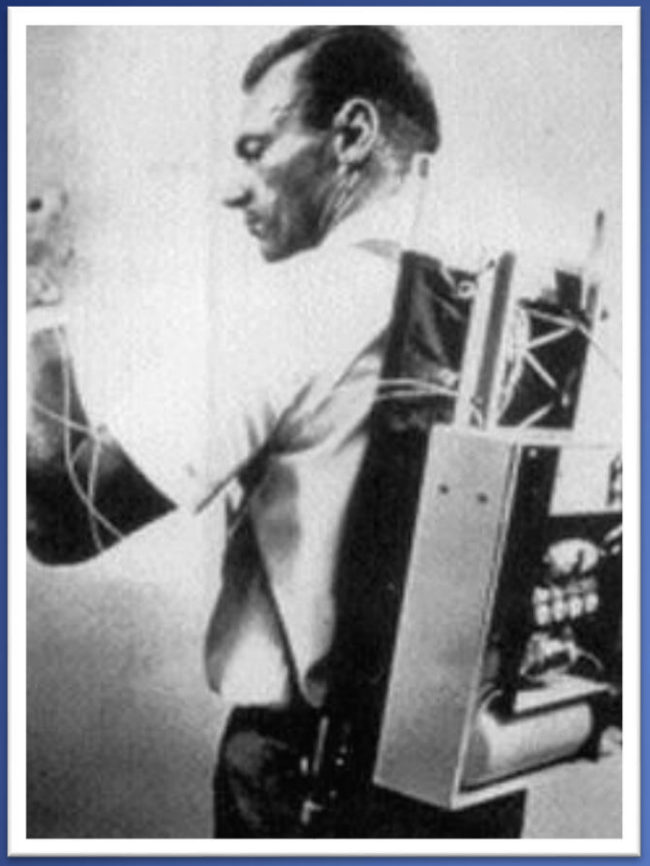


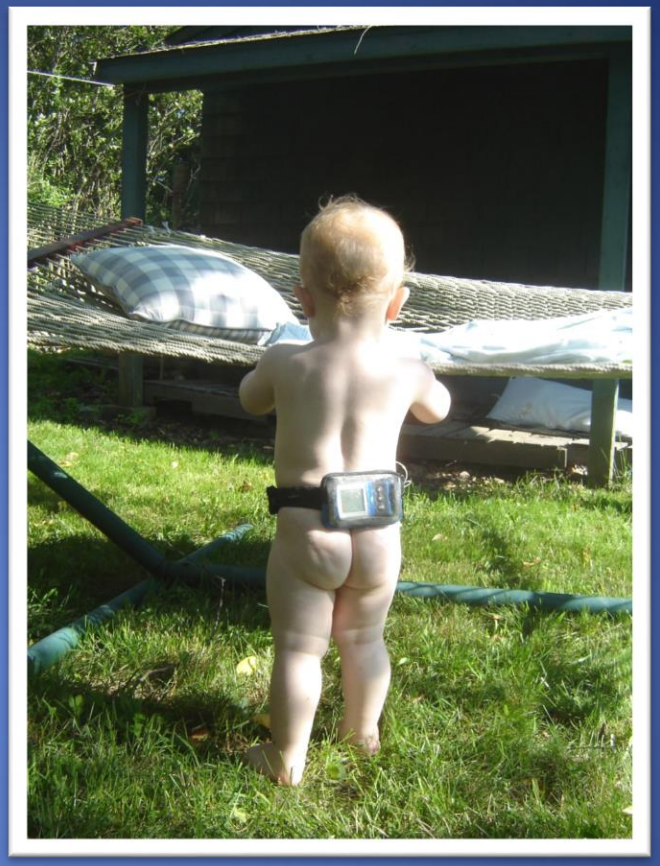
Summary: Clinical Challenges T1D

- Transitions are challenging: growing older, adolescence, early childhood
- Psychosocial barriers to adherence
- Hypoglycemia
- Burden of current management is high

Future Directions for T1D

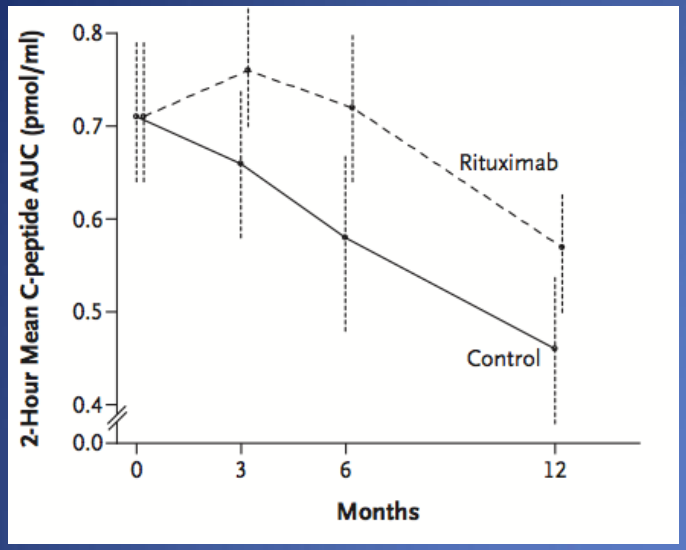
- Technological “cure”
- Biological cure

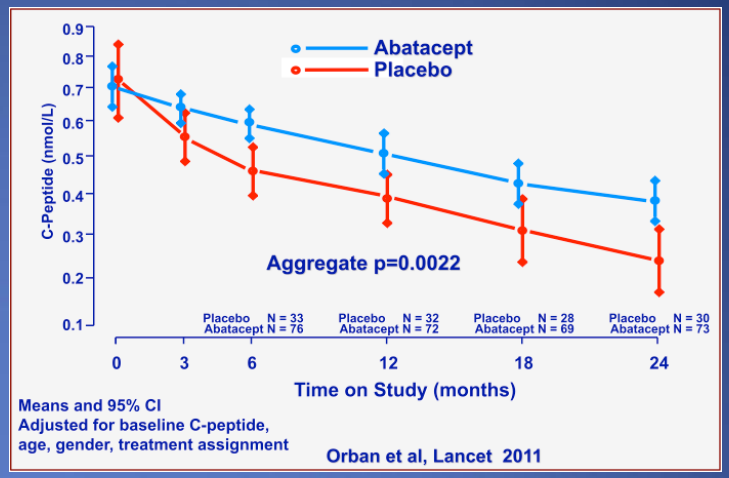


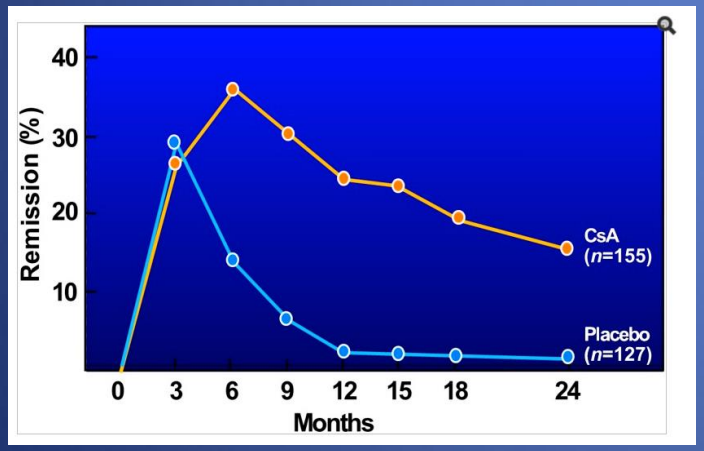


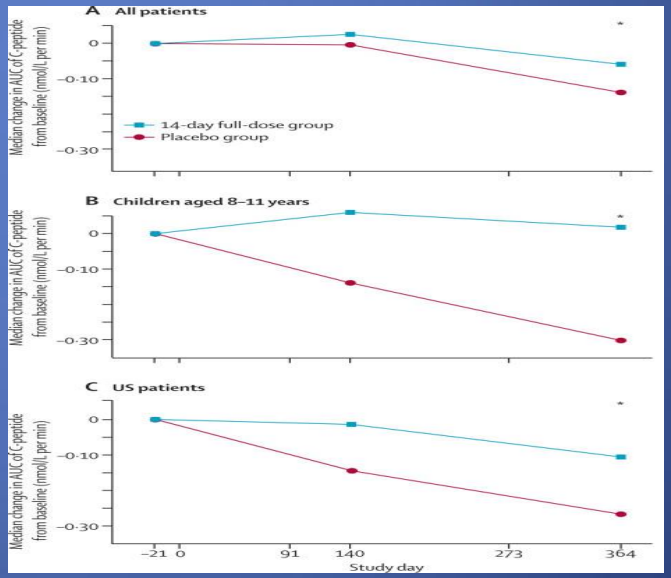

Carrier
11:19 AM
123 mg/dl
0.59 Insulin
1.07 Glucagon
BOSTON UNIVERSITY

New Onset T1D Trials – Moderate Success

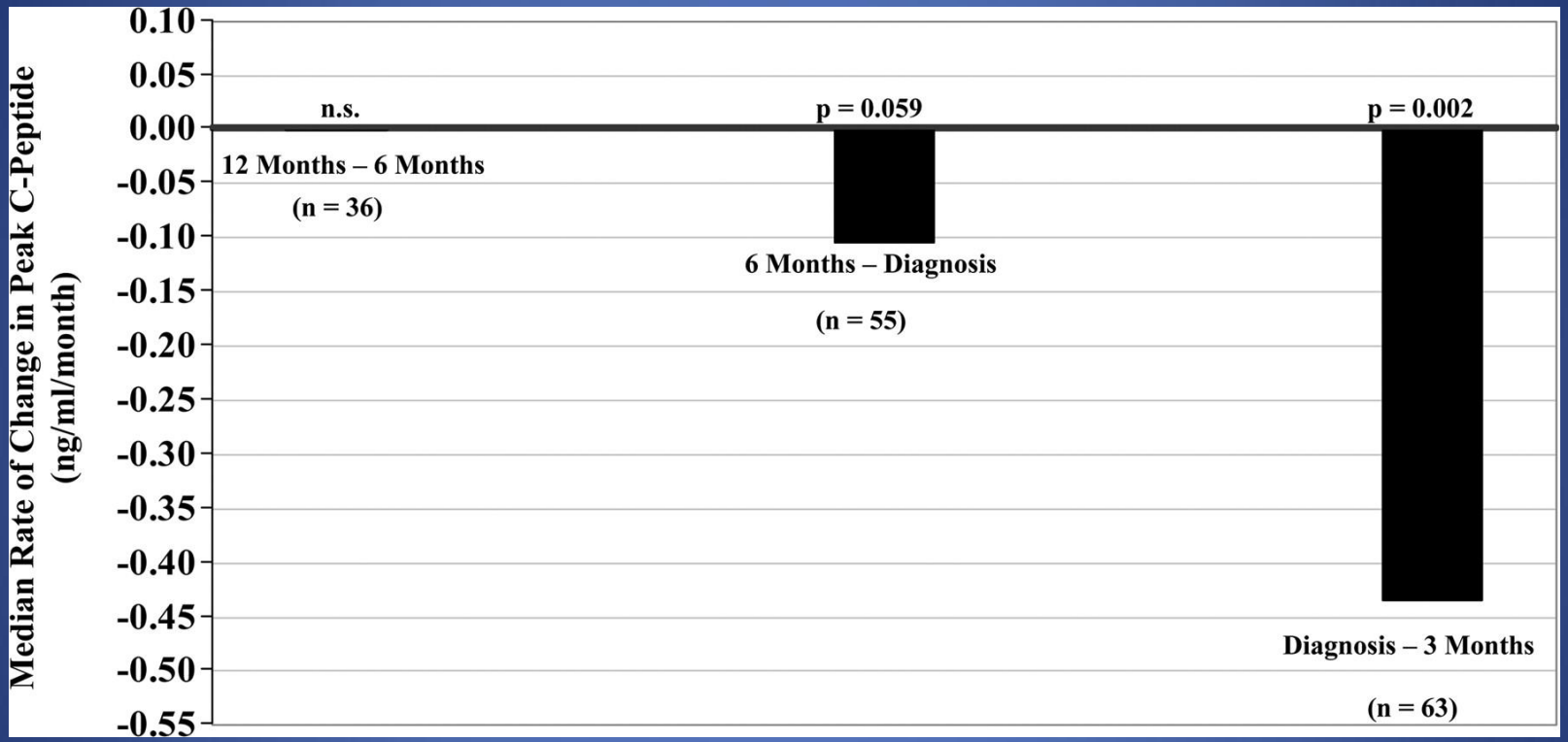






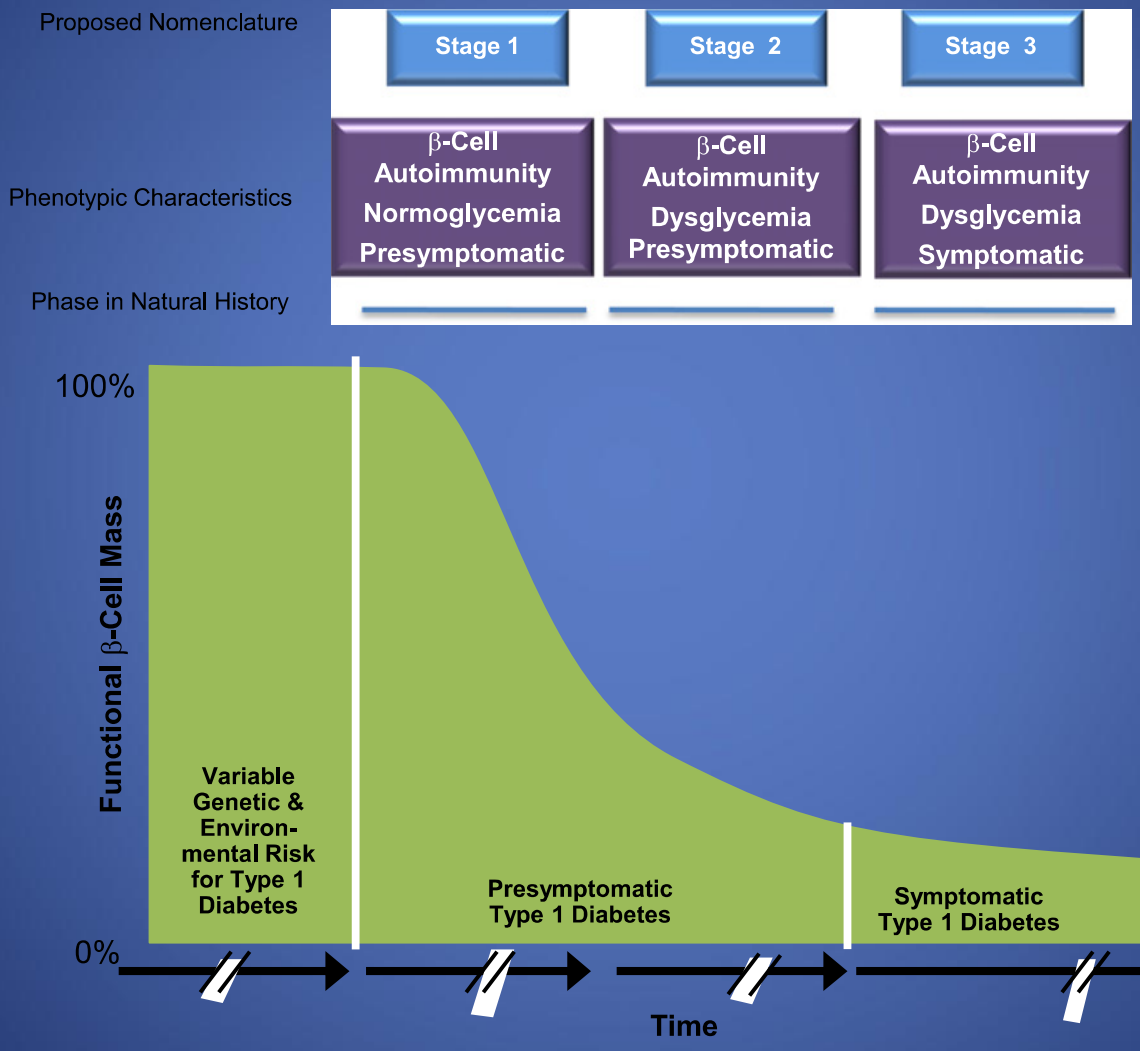


Fall in C-Peptide Prior to T1D Diagnosis



Sosenko, 2008

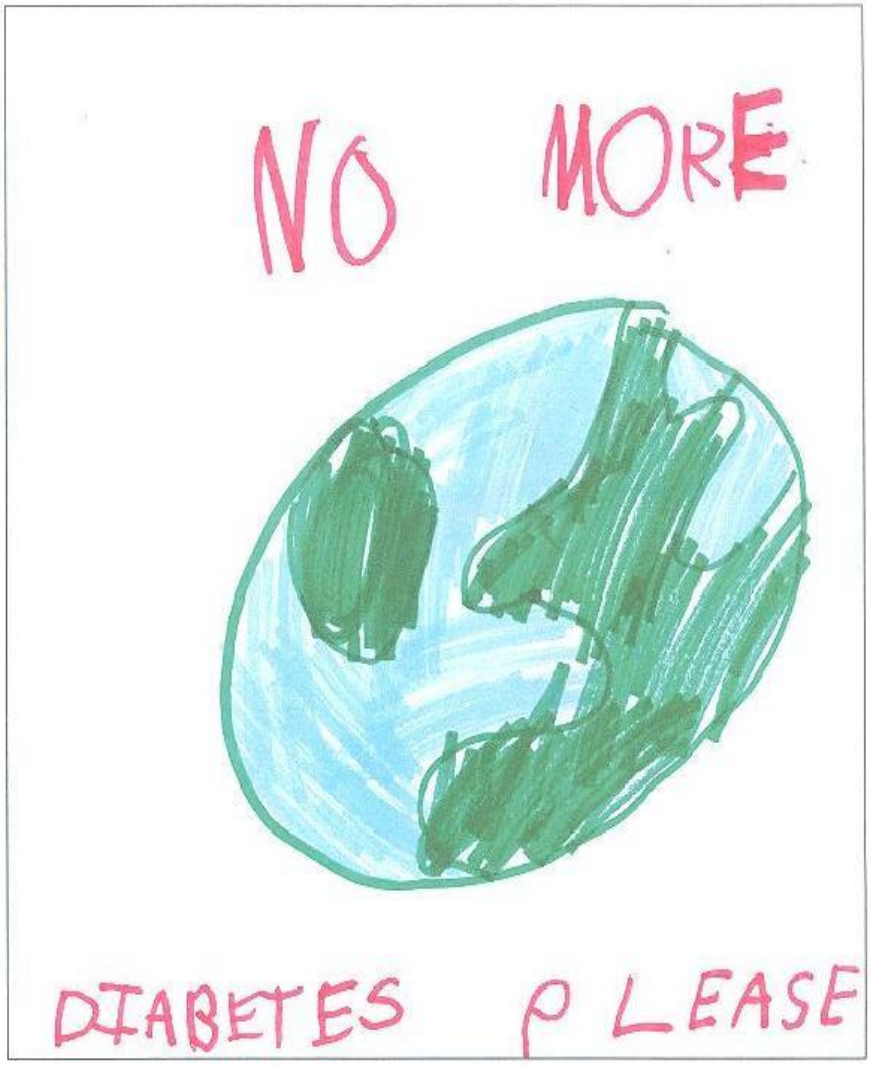
NIH TrialNet: Proposed T1D Stages



Insel 2015

Early T1D Diagnosis and Treatment

- Early diagnosis and management T1D optimal
- Early metabolic control to preserve c-peptide, associated with better outcomes, less hypoglycemia, fewer long-term complications
- Research screening of relatives through NIH TrialNet recommended. Two antibodies very high risk for T1D development
- T1D screening associated with DKA prevention (NIH TEDDY Study)
- Future participation in prevention and treatment trials



The Earth would be a better place
without diabetes.