Diabetes Type 1

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What is Diabetes ?

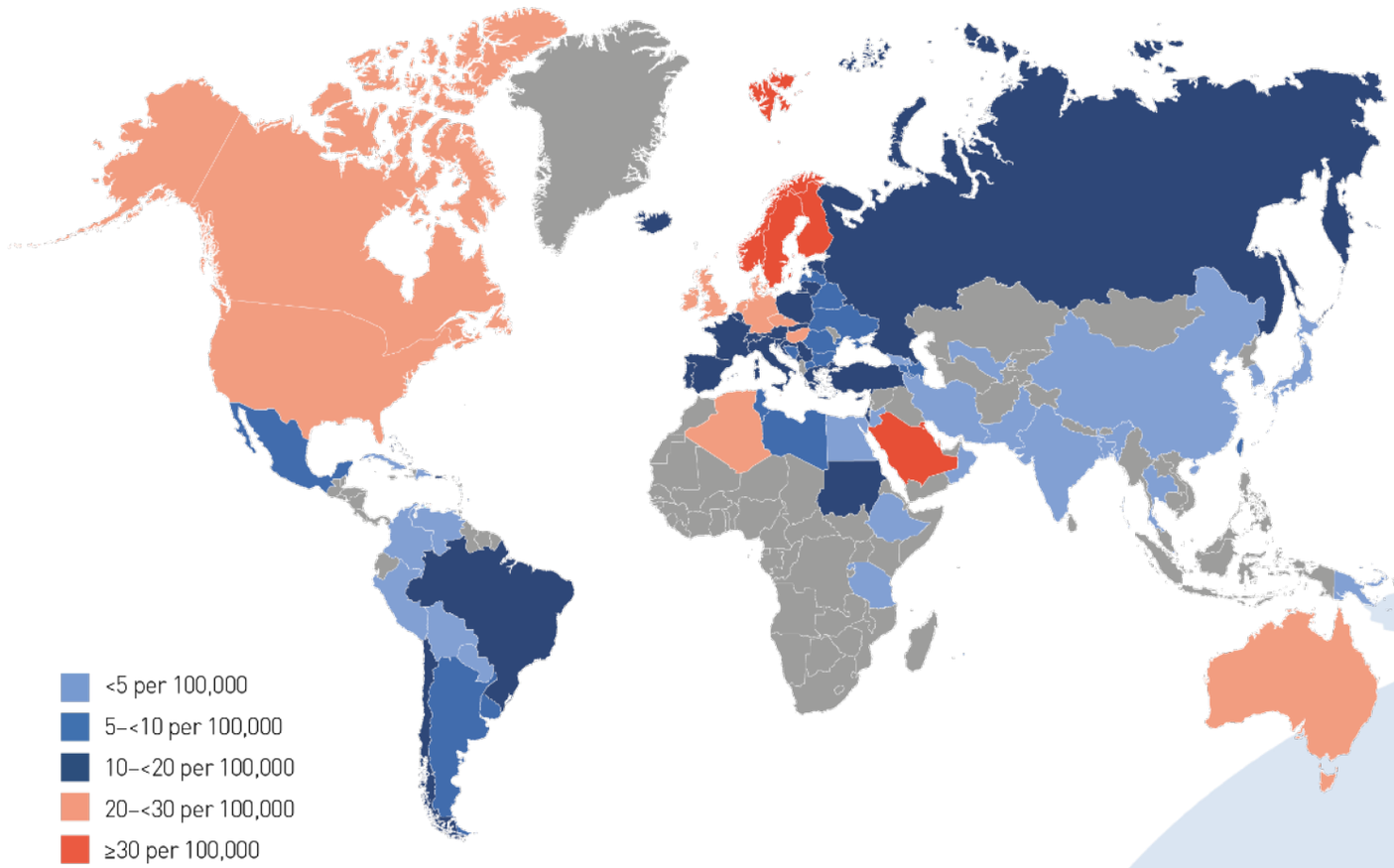
Diabetes is a complex, chronic illness requiring continuous medical care with ***multifactorial risk-reduction strategies beyond glycemic control***. Ongoing patient self-management education and support are critical to preventing acute complications and reducing the risk of long-term complications

American diabetes Association. Standards of medical care in diabetes--2015

DM Epidemiology and Burden

CHILDREN AND ADOLESCENTS

Age-sex standardised incidence rates (per 100,000 population per annum) of type 1 diabetes in children and adolescents aged 0–14 years, 2019

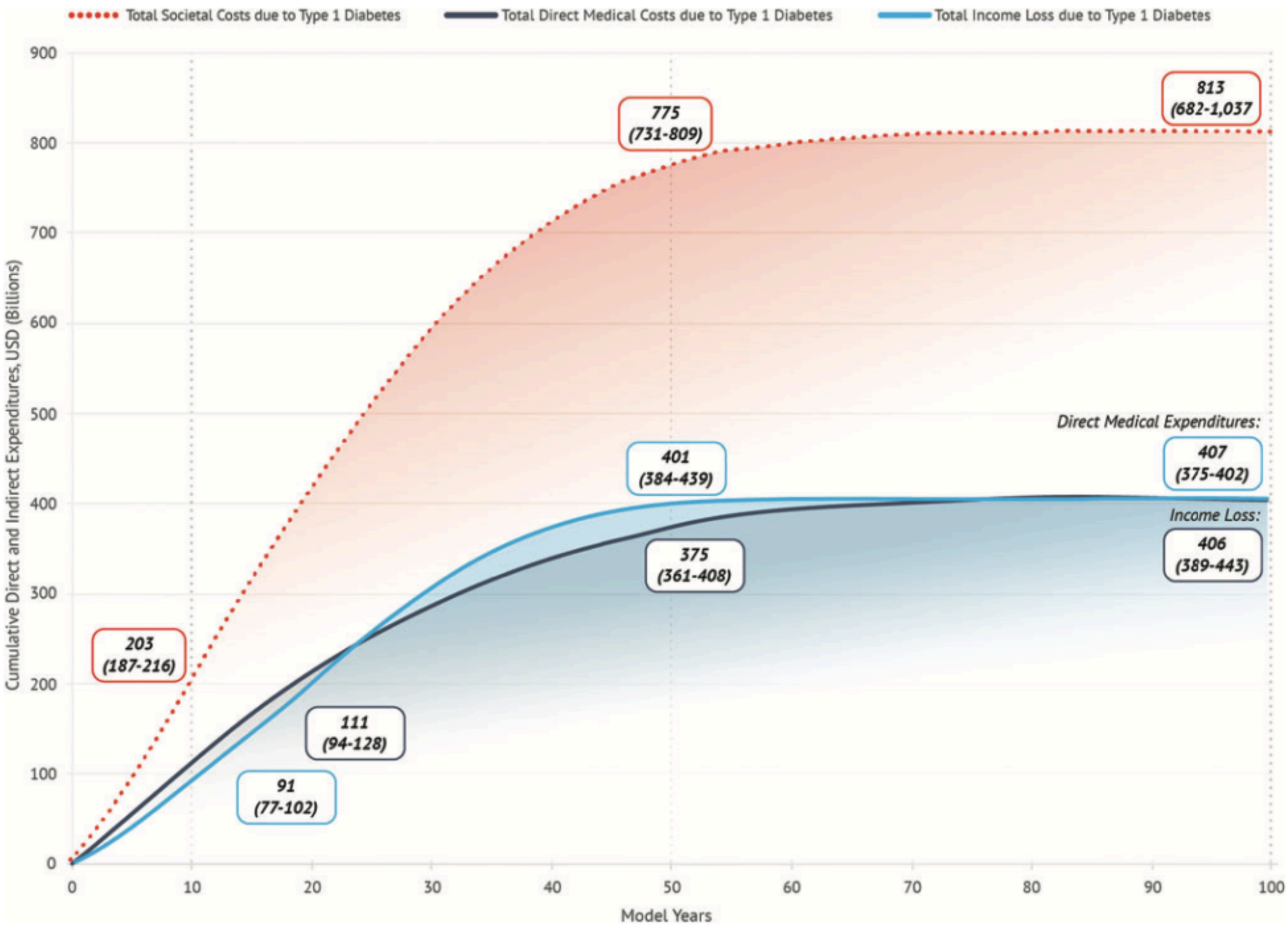


International Diabetes Federation

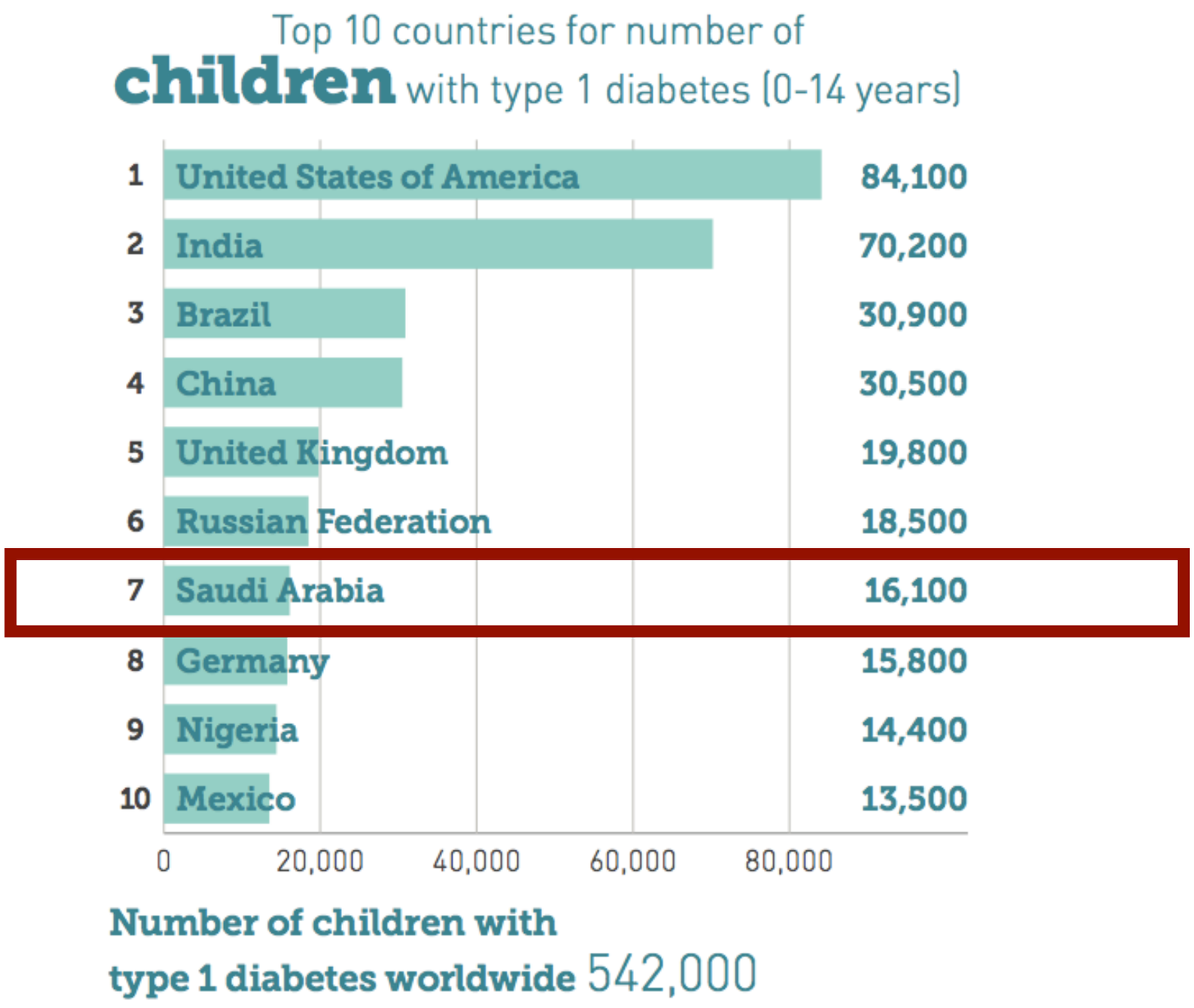
Table 3.16 **Top 10 countries or territories for the incidence rates (per 100,000 population per annum) of type 1 diabetes in children (aged 0–14 years)**

Rank	Country or territory	Incidence rates (per 100,000 population per year) 0–14 years
1	Finland	62.3
2	Sweden	43.2
3	Kuwait	41.7
4	Norway	33.6
5	Saudi Arabia	31.4
6	Canada	29.9
7	United Kingdom	29.4
8	Qatar	28.4
9	Ireland	27.5
10	Denmark	27.0

IDF Diabetes Atlas | 9th edition


Total Societal Costs due to Type 1 Diabetes
Total Direct Medical Costs due to Type 1 Diabetes
Total Income Loss due to Type 1 Diabetes
Cumulative Direct and Indirect Expenditures, USD (Billions)
Model Years
775 (731-809)
813 (682-1,037
Direct Medical Expenditures:
401 (384-439)
407 (375-402)
Income Loss:
375 (361-408)
406 (389-443)
203 (187-216)
111 (94-128)
91 (77-102)

Children with diabetes



International Diabetes Federation. IDF Diabetes Atlas, 7th edn. Brussels, Belgium: International Diabetes Federation, 2015. http://www.diabetesatlas.org

- Diabetes was the ***<u>7th leading cause of death</u>*** in 2010 behind Ischemic heart disease (1st leading cause) and chronic Kidney disease (6th leading cause).

Burden of Disease, Injuries, and Risk Factors in the Kingdom of Saudi Arabia, 1990-2010. *Prev Chronic Dis*. 2014

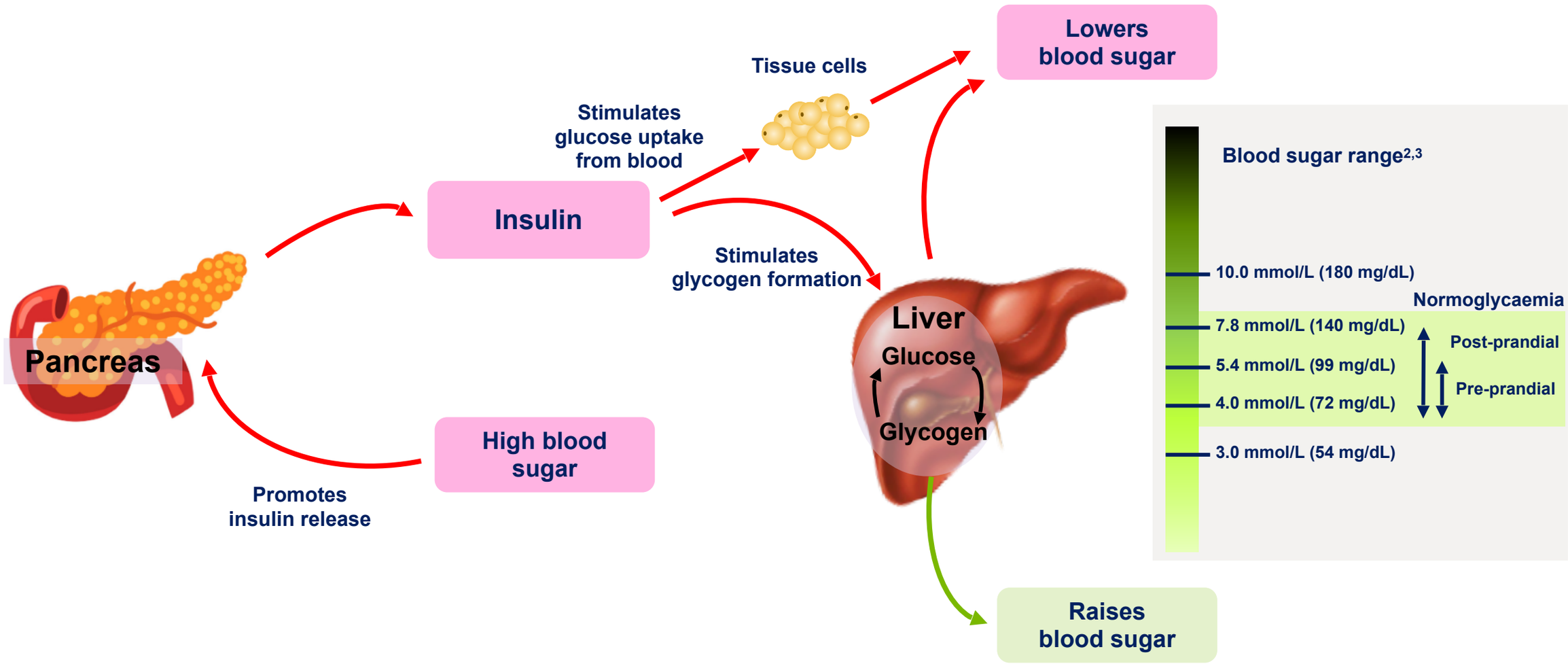
Table 2. Leading Causes of Disability-Adjusted Life Years by Sex, Kingdom of Saudi Arabia, 1990, 2005, and 2010

	1990			2005			2010		
Rank	Male (%)	Female (%)	Total (%)	Male (%)	Female (%)	Total (%)	Male (%)	Female (%)	Total (%)
1	Preterm birth complications (12.04%)	Preterm birth complications (12.35%)	Preterm birth complications (12.17%)	Road traffic injury (12.00%)	Major depressive disorder (7.56%)	Road traffic injury (8.55%)	Road traffic injury (12.40%)	Major depressive disorder (7.88%)	Road traffic injury (8.63%)
2	Road traffic injury (11.04%)	Congenital anomalies (7.65%)	Road traffic injury (7.79%)	Ischemic heart disease (7.38%)	Preterm birth complications (6.94%)	Preterm birth complications (6.38%)	Ischemic heart disease (7.46%)	Preterm birth complications (5.58%)	Ischemic heart disease (6.23%)
3	Ischemic heart disease (6.03%)	Major depressive disorder (5.72%)	Congenital anomalies (6.53%)	Preterm birth complications (6.00%)	Diabetes mellitus (4.71%)	Ischemic heart disease (6.12%)	Diabetes mellitus (5.79%)	Diabetes mellitus (5.10%)	Major depressive disorder (5.87%)
4	Congenital anomalies (5.71%)	Iron-deficiency anemia (3.86%)	Ischemic heart disease (5.09%)	Low back pain (5.37%)	Low back pain (4.64%)	Major depressive disorder (5.61%)	Low back pain (5.77%)	Low back pain (5.06%)	Diabetes mellitus (5.51%)
5	Low back pain (3.88%)	Ischemic heart disease (3.78%)	Major depressive disorder (4.43%)	Diabetes mellitus (5.26%)	Congenital anomalies (4.54%)	Low back pain (5.08%)	Preterm birth complications (4.79%)	Ischemic heart disease (4.46%)	Low back pain (5.48%)
6	Major depressive disorder (3.51%)	Lower respiratory infections (3.69%)	Low back pain (3.51%)	Major depressive disorder (4.29%)	Ischemic heart disease (4.26%)	Diabetes mellitus (5.04%)	Major depressive disorder (4.47%)	Anxiety disorders (4.30%)	Preterm birth complications (5.11%)
7	Lower respiratory infections (2.94%)	Diarrheal diseases (3.41%)	Lower respiratory infections (3.26%)	Cerebrovascular disease (3.54%)	Anxiety disorders (4.10%)	Congenital anomalies (3.79%)	Cerebrovascular disease (3.46%)	Iron deficiency anemia (3.75%)	Cerebrovascular disease (3.44%)
8	Cerebrovascular disease (2.77%)	Road traffic injury (3.28%)	Iron deficiency anemia (3.09%)	Congenital anomalies (3.28%)	Iron deficiency anemia (3.89%)	Cerebrovascular disease 3.41%)	Drug-use disorders (2.75%)	Congenital anomalies (3.48%)	Congenital anomalies (2.97%)
9	Neonatal encephalopathy (2.62%)	Cerebrovascular disease (3.27%)	Cerebrovascular disease (2.98%)	Drug-use disorders (2.31%)	Road traffic injury (3.48%)	Iron deficiency anemia (2.81%)	Congenital anomalies (2.62%)	Cerebrovascular disease (3.41%)	Anxiety disorders (2.88%)
10	Diabetes mellitus (2.62%)	Low back pain (3.00%)	Diarrheal diseases (2.86%)	Iron deficiency anemia (2.08%)	Cerebrovascular disease (3.22%)	Anxiety disorders (2.77%)	Iron deficiency anemia (1.92%)	Road traffic injury (3.20%)	Iron deficiency anemia (2.67%)

Burden of Disease, Injuries, and Risk Factors in the Kingdom of Saudi Arabia, 1990-2010. *Prev Chronic Dis*. 2014

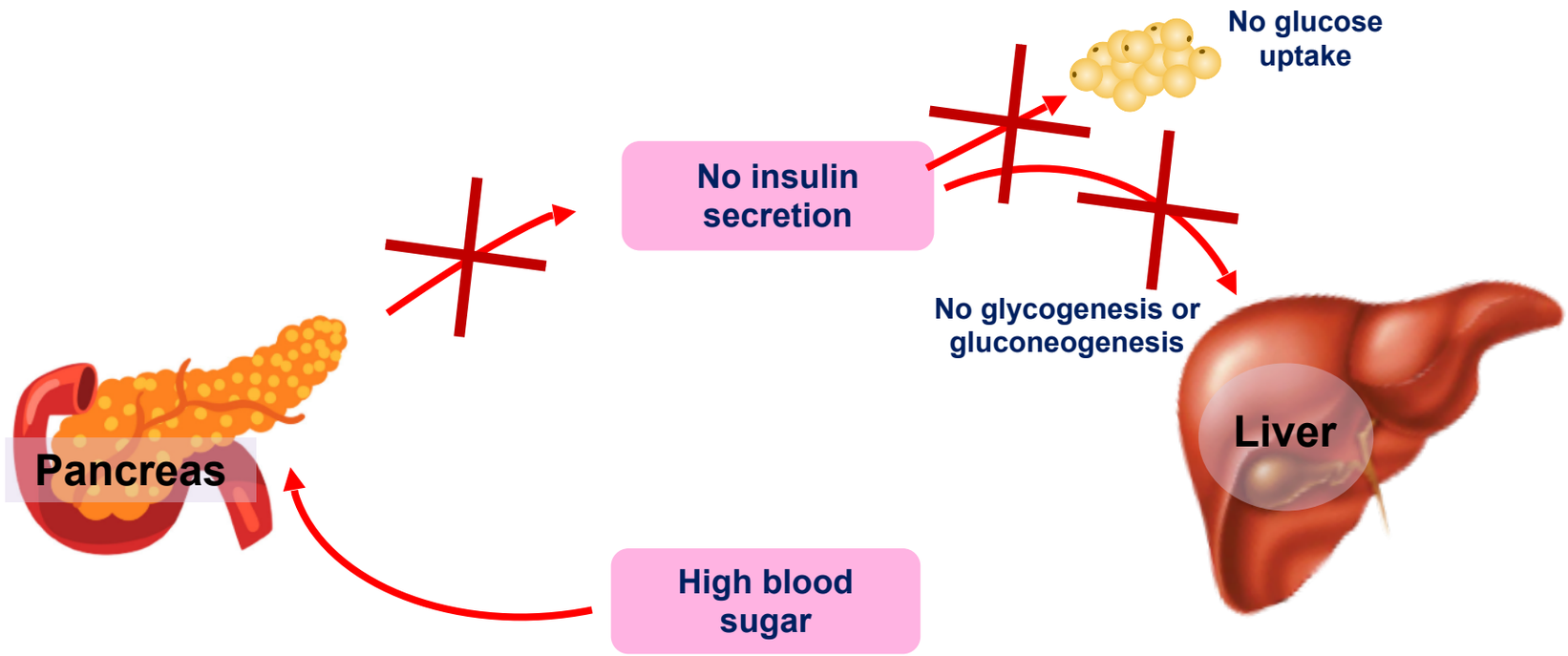
Insulin Action and Glucose Homeostasis

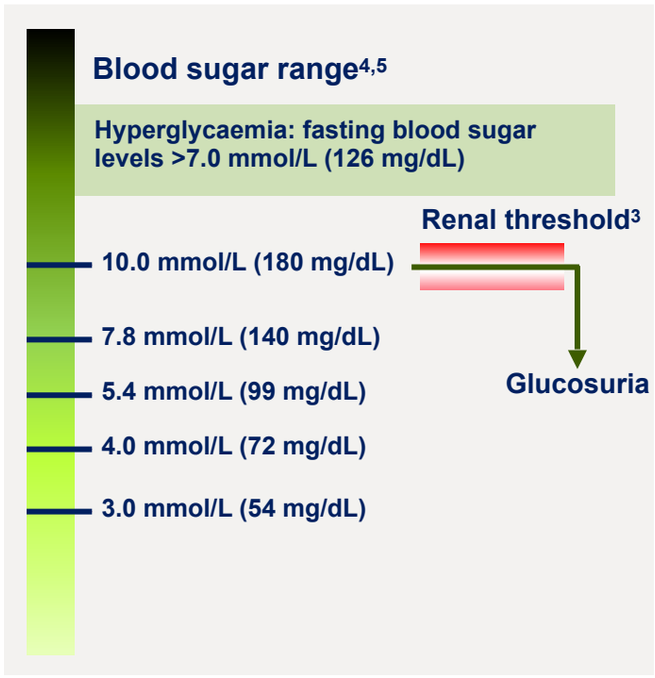
Regulation of insulin and glucose in normal physiology[1,2]



1. Adapted from Roder PV, et al. *Exp Mol Med* 2016;48:e129; 2. Diabetes.co.uk. Blood Sugar Level Ranges. Available at: https://www.diabetes.co.uk/diabetes_care/blood-sugar-level-ranges.html (Accessed March 2019); 3. International Hypoglycaemia Study Group. *Diabetes Care* 2017;40:155–157

Regulation of insulin and glucose in Type 1 diabetes[1–3]





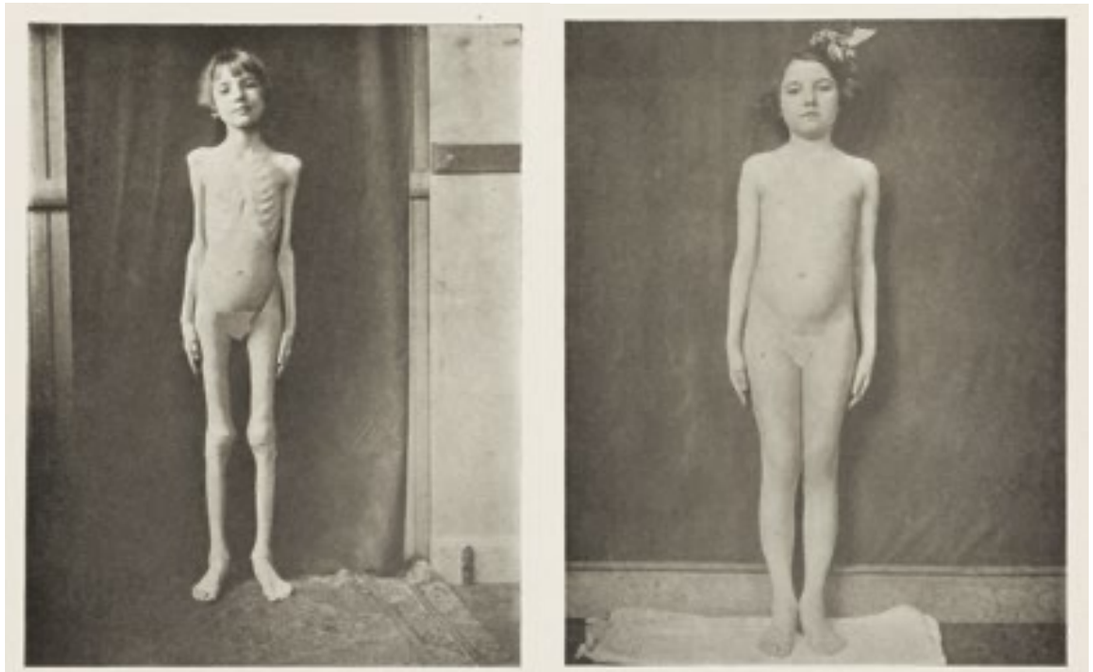
Insufficient endogenous insulin production increases blood sugar levels and may lead to glucosuria when exceeding the renal threshold

1. Adapted from Roder PV, et al. *Exp Mol Med* 2016;48:e129; 2. Atkinson MA, et al. *Lancet* 2014;383:69–82; 3. Ferrannini E. *Diabetes* 2011;60:695–696; 4. Diabetes.co.uk. Blood Sugar Level Ranges. Available at: https://www.diabetes.co.uk/diabetes_care/blood-sugar-level-ranges.html (Accessed March 2019); 5. International Hypoglycaemia Study Group. *Diabetes Care* 2017;40:155–157

Insulin is necessary for survival

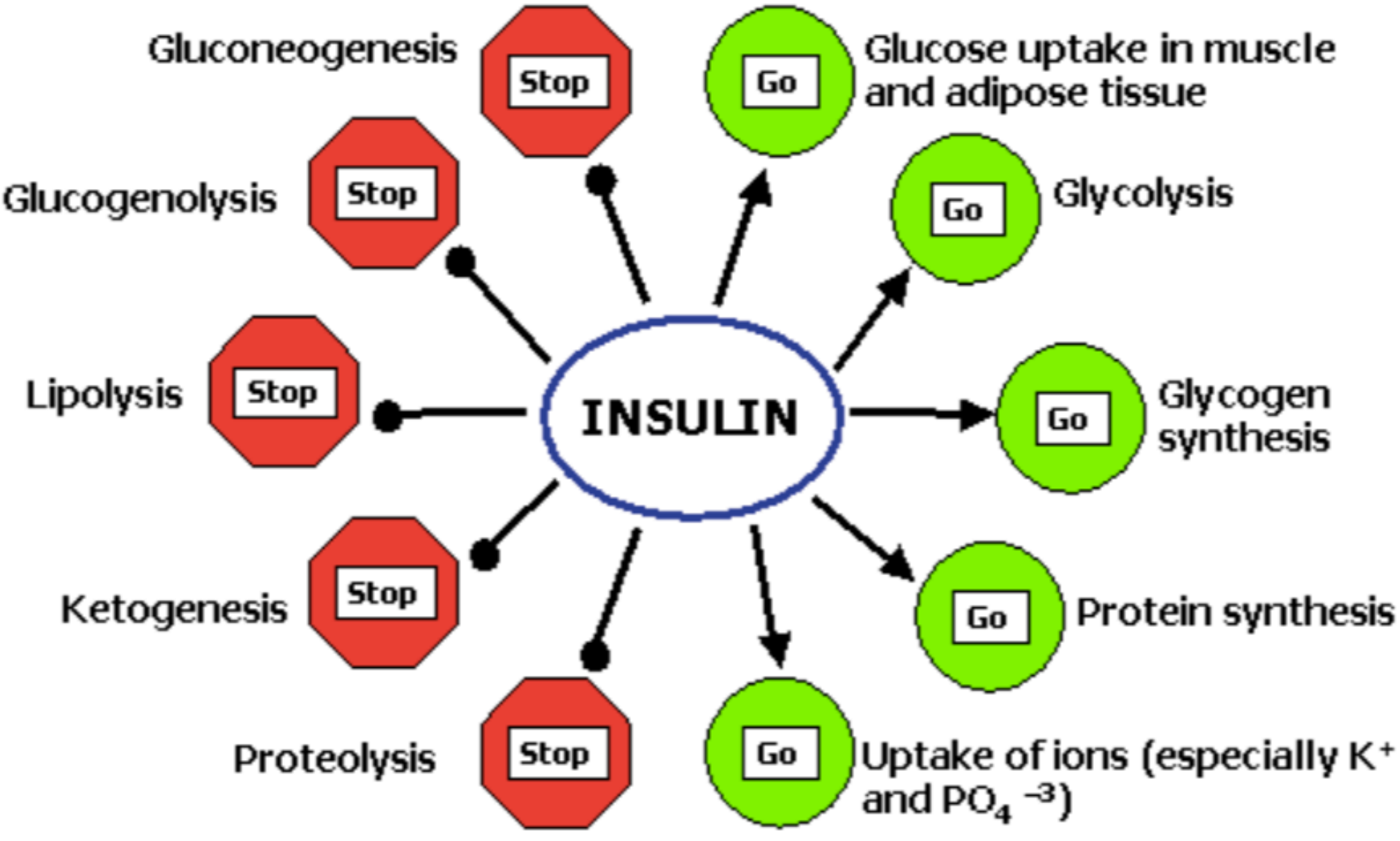
- Type 1 diabetes is an autoimmune disease leading to β-cell destruction, lack of insulin production and a need for life-long insulin therapy[1]
- Until 1922, the treatment for Type 1 diabetes was a ‘starvation diet’ – reducing patients to emaciation and subjecting them to a life of misery[2]
- The work of John Macleod, Frederik Banting and Charles Best with their patient, Elizabeth Hughes (right), led to the widespread use of insulin injections as a treatment for Type 1 diabetes[2]

Insulin treatment allows for a dramatic recovery in patients with Type 1 diabetes[2]



1. Atkinson MA, et al. *Lancet* 2014;383:69–82; 2. Botting JH. *Animal and Medicine.* Cambridge, Open Book Publishers; 2015:143–154

Actions of Insulin



Classification of Diabetes and Diagnosis criteria

Classification of Diabetes

- **Type 1 diabetes** (due to b-cell destruction, leading to absolute insulin deficiency)

- **Type 2 diabetes** (due to a progressive insulin secretory defect on the background of insulin resistance)

- **Gestational diabetes mellitus** (GDM) (diabetes diagnosed in the second or third trimester of pregnancy that is not clearly overt diabetes)

- **Specific types of diabetes** due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young [MODY]), diseases of the exocrine pancreas (such as cystic fibrosis), and drug or chemical induced diabetes (such as in the treatment of HIV/AIDS or after organ transplantation)

American diabetes Association. Standards of medical care in diabetes--2015

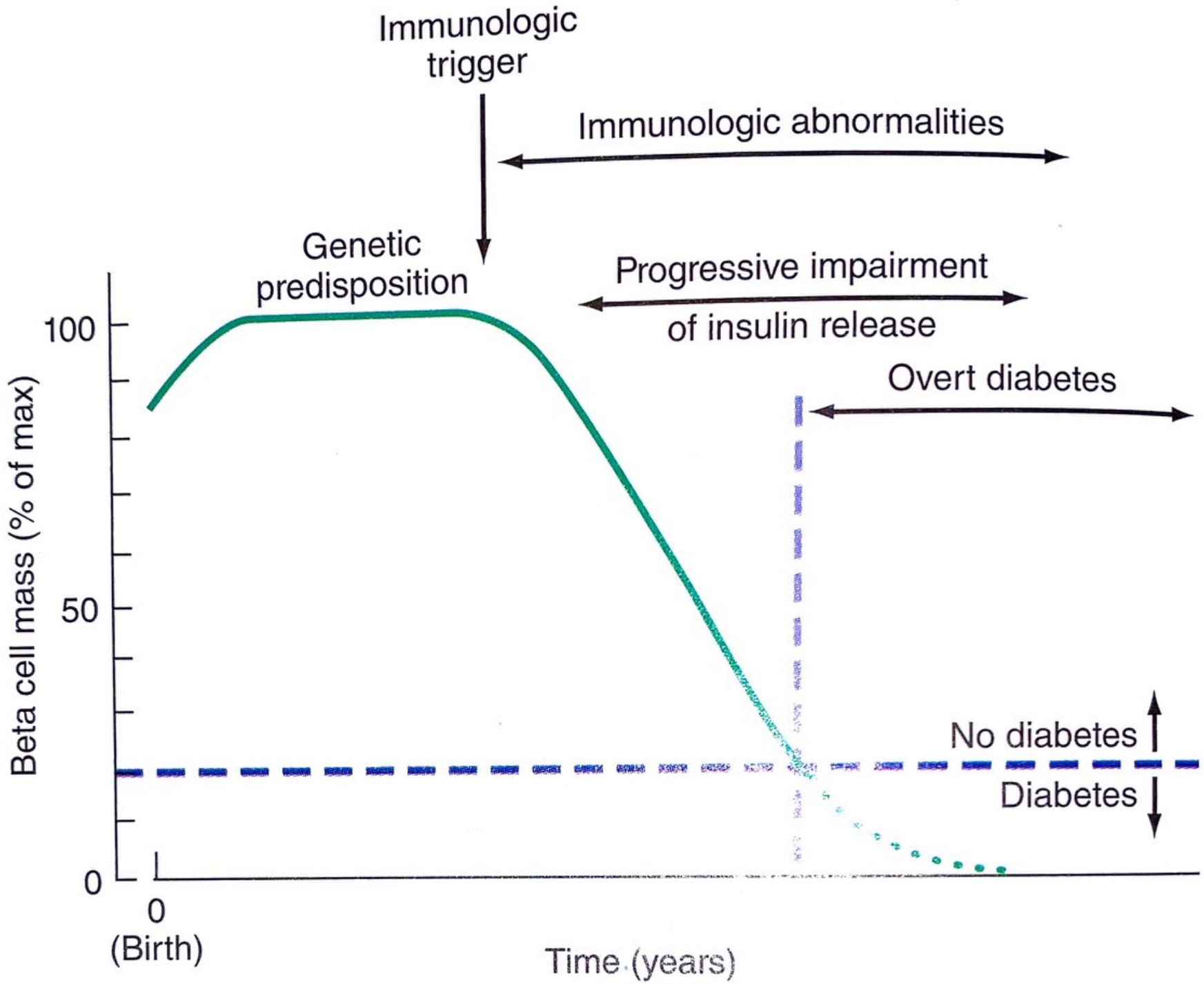
Type of Diabetes	Normal glucose tolerance	Hyperglycemia		
		Pre-diabetes*	Diabetes Mellitus	
		Impaired fasting glucose or impaired glucose tolerance	Not insulin requiring	Insulin required for control / Insulin required for survival
Type 1				
Type 2				
Other specific types				
Gestational Diabetes				
Time (years)				
FPG	<5.6 mmol/L (100 mg/dL)	5.6–6.9 mmol/L (100–125 mg/dL)	≥7.0 mmol/L (126 mg/dL)	
2-h PG	<7.8 mmol/L (140 mg/dL)	7.8–11.0 mmol/L (140–199 mg/dL)	≥11.1 mmol/L (200 mg/dL)	
HbA1C	<5.6%	5.7–6.4%	≥6.5%	

Pathogenesis of T1DM

- T1DM is the result of interactions of genetic, environmental, and immunological factors that ultimately lead to the destruction of the pancreatic Beta cells and insulin deficiency.

- It can develop at any age, but most commonly < 30

- Most, but not all, individuals have evidence of islet-directed autoimmunity


Immunologic trigger
Immunologic abnormalities
Genetic predisposition
Progressive impairment of insulin release
Overt diabetes
100
50
0
Beta cell mass (% of max)
No diabetes
Diabetes
0 (Birth)
Time (years)

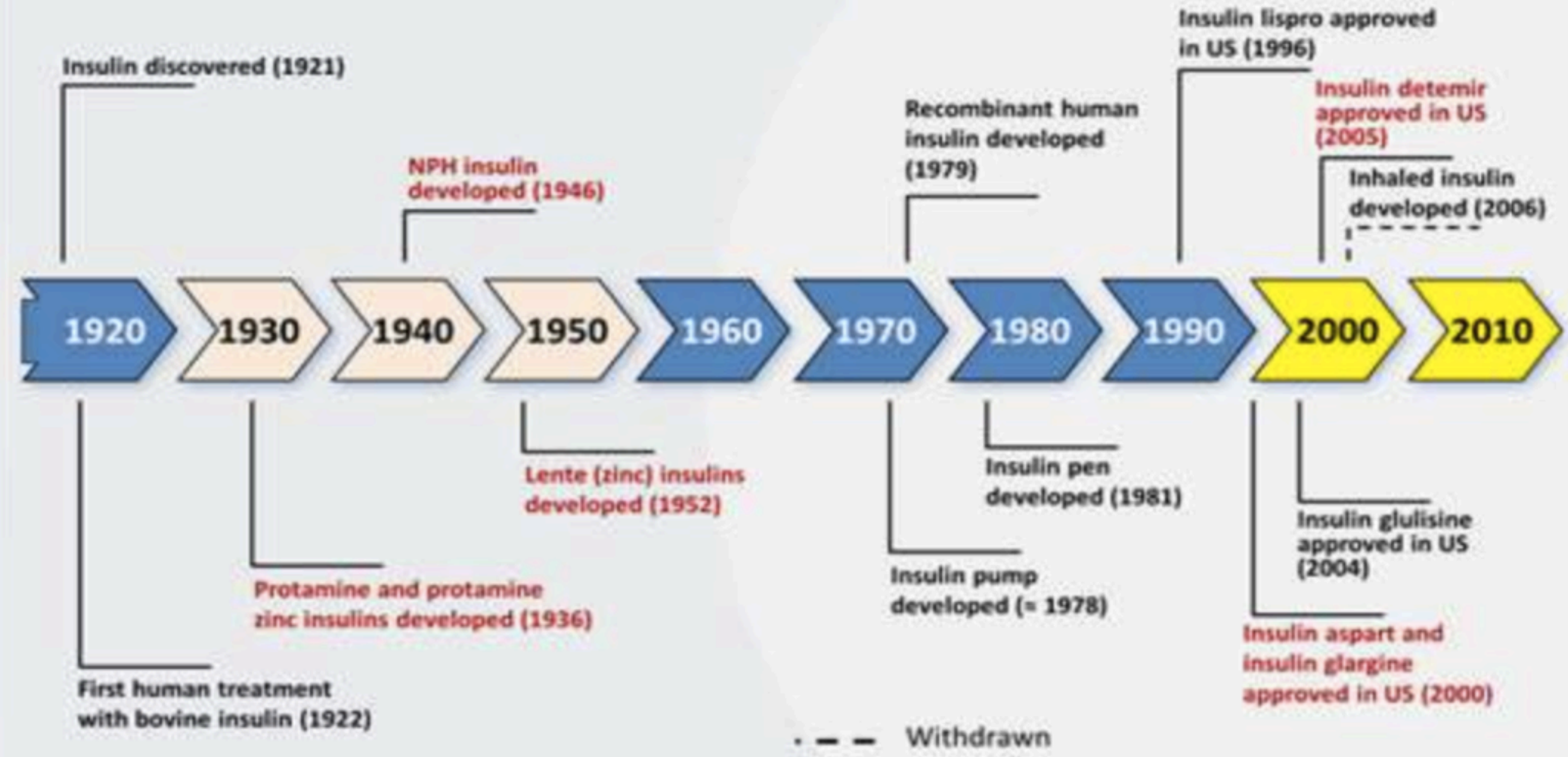
Presentation of T1DM

Figure 1.2 **The typical symptoms of type 1 diabetes**

Management

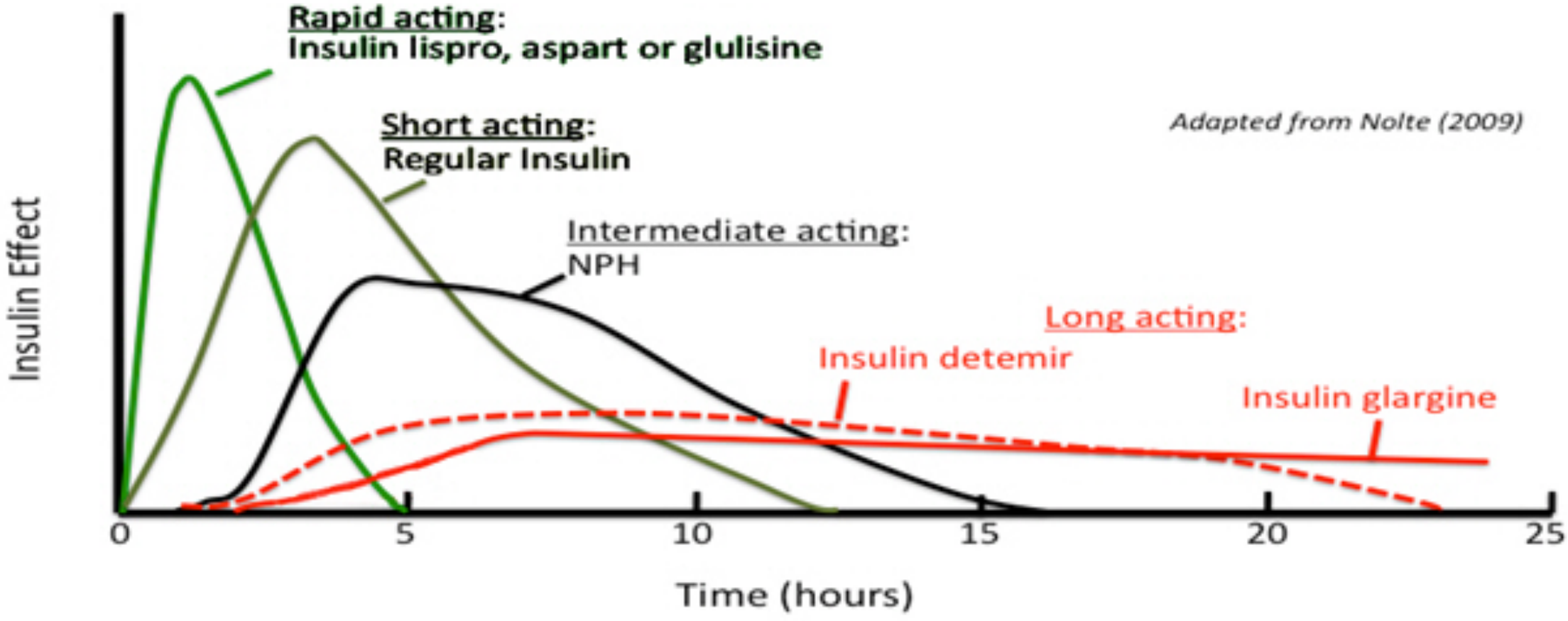
- **Goals of Therapy**
  - Eliminate symptoms related to hyperglycaemia
  - Reduce risk or eliminate diabetes complications
  - Allow patient to achieve as normal a lifestyle as possible

Milestones in Insulin Development



Tattersall RB. In: Pickup JC, Williams G, eds. Textbook of Diabetes. 3rd ed. Blackwell Science: Malden, MA; 2003:1.1-1.22; Drugs@ FDA; Bailey CJ, Barnett AH. *BMJ.* 2007;335:1156.

Insulin Types, Duration



Adapted from Nolte (2009)

Available Therapeutic Regimens

- **CT** = Conventional Therapy
  (1 or 2 injections / day)

- **MDI** = Multiple Daily Injections
  (3 – 6 injections / day)

- **CSII** = Continuous S.C Insulin Infusion "Insulin Pump"

Types of insulin			
Insulin type (trade name)	**Onset**	**Peak**	**Duration**
Bolus (preprandial or mealtime) insulins			
Rapid-acting insulin analogues (clear) • Insulin aspart (NovoRapid®) • Insulin glulisine (Apidra®) • Insulin lispro (Humalog®) U-100 U-200 • Faster-acting insulin aspart (Fiasp®)	 9–20min 10–15min 10–15min 4min	 1–1.5h 1–1.5h 1–2h 0.5-1.5h	 3–5h 3.5–5h 3–4.75h 3-5h
Short-acting insulins (clear) • Insulin regular [Humulin®-R, Novolin® ge Toronto] • Insulin regular [Entuzity® (U-500)]	 30min 15min	 2–3h 4-8h	 6.5h 17-24h
Basal insulins			
Intermediate-acting (cloudy) • Insulin neutral protamine Hagedorn (Humulin® -N, Novolin® ge NPH)	1–3h	5–8h	Up to 18h
Long-acting insulin (clear) • Insulin detemir (Levemir®) • Insulin glargine U-100 (Lantus®) • Insulin glargine U-300 (Toujeo®) • Insulin glargine biosimilar (Basaglar®) • Degludec U-100, U-200 (Tresiba®)	90min	Not applicable	U-100 glargine 24h, detemir 16–24h U-300 glargine >30h degludec 42h

Types of insulin			
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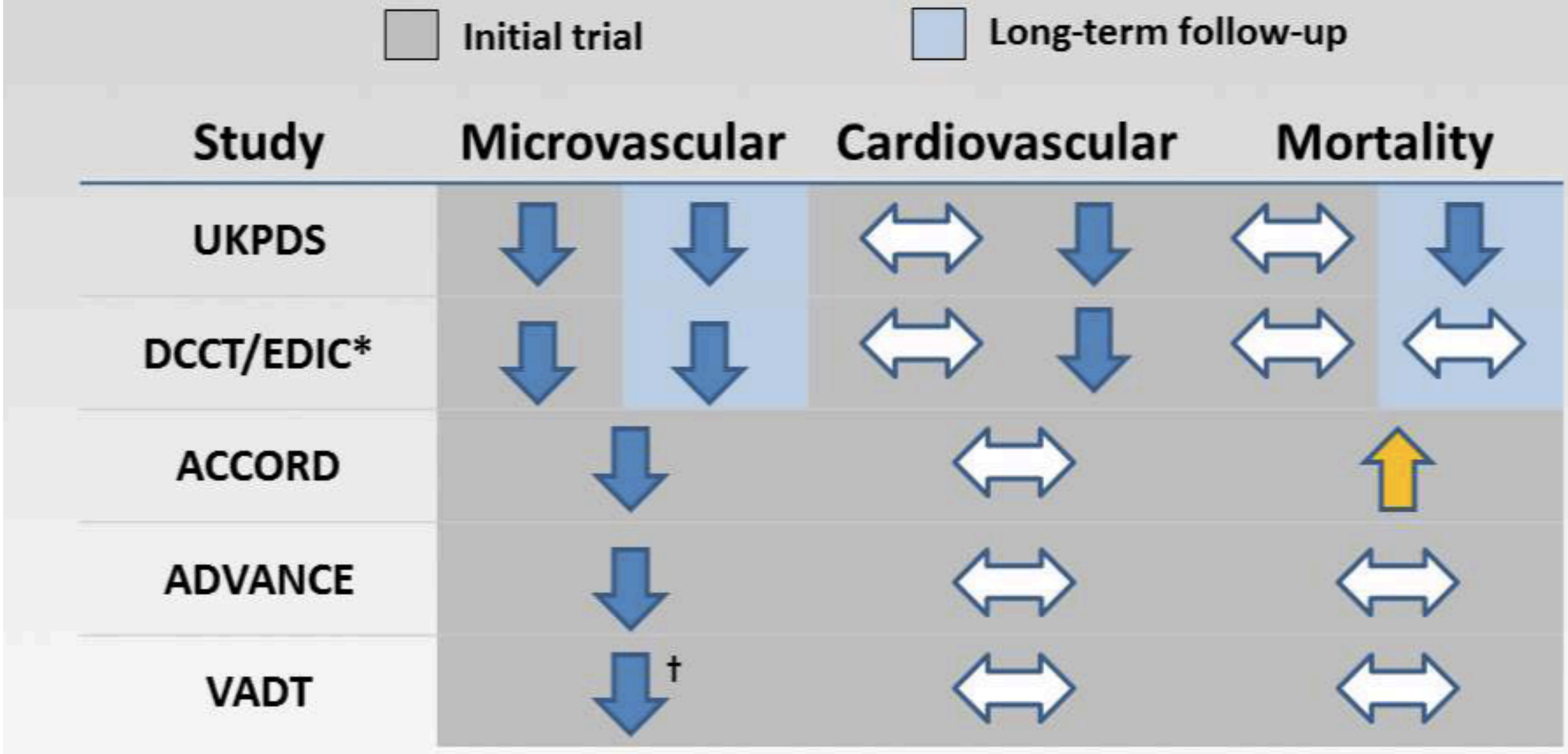
Short-acting insulins (clear) • Insulin regular [Humulin®-R, Novolin® ge Toronto] • Insulin regular [Entuzity® (U-500)]	 30min 15min	 2–3h 4-8h	 6.5h 17-24h
Basal insulins			
Intermediate-acting (cloudy) • Insulin neutral protamine Hagedorn (Humulin® -N, Novolin® ge NPH)	1–3h	5–8h	Up to 18h
Long-acting insulin (clear) • Insulin detemir (Levemir®) • Insulin glargine U-100 (Lantus®) • Insulin glargine U-300 (Toujeo®) • Insulin glargine biosimilar (Basaglar®) • Degludec U-100, U-200 (Tresiba®)	90min	Not applicable	U-100 glargine 24h, detemir 16–24h U-300 glargine >30h degludec 42h

Premixed insulins	
Premixed regular insulin –NPH (cloudy) • Humulin® 30/70 • Novolin® ge 30/70, 40/60, 50/50	A single vial or cartridge contains a fixed ratio of insulin
Premixed insulin analogues (cloudy) • Biphasic insulin aspart (NovoMix® 30) • Insulin lispro/lispro protamine (Humalog® Mix25 and Mix50)	(% of rapid-acting or short-acting insulin to % of intermediate-acting insulin)

Impact of Intensive Therapy for Diabetes:
Summary of Major Clinical Trials



Adapted from: Kendall DM, et al. International Diabetes Center. 2009; UKPDS Group. *Lancet.* 1998;352:854; Holman RR, et al. *N Engl J Med*. 2008;359:1577; DCCT Research Group. *N Engl J Med.* 1993;329;977; Nathan DM, et al. *N Engl J Med*. 2005;353:2643; Gerstein HC, et al. *N Engl J Med.* 2008;358:2545; Patel A, et al. *N Engl J Med.* 2008;358:2560; Duckworth W, et al. *N Engl J Med.* 2009;360:129; Beigi FI, et al. *Lancet.* 2010;376:419-3.

*In T1DM
†Albuminuria reduction

KEY MESSAGES

- Basal-bolus insulin therapies (i.e. multiple daily injections or continuous subcutaneous insulin infusion) are the preferred insulin management regimens for adults with type 1 diabetes.
- Insulin regimens should be tailored to the individual's treatment goals, lifestyle, diet, age, general health, motivation, hypoglycemia awareness status and ability for self-management.
- All individuals with type 1 diabetes should be counselled about the risk, prevention and treatment of hypoglycemia. Avoidance of nocturnal hypoglycemia may include changes in insulin therapy and increased monitoring.
- If glycemic targets are not met with optimized multiple daily injections, continuous subcutaneous insulin infusion may be considered. Successful continuous subcutaneous insulin infusion therapy requires appropriate candidate selection, ongoing support and frequent involvement with the healthcare team.
- Continuous glucose monitoring may be offered to people not meeting their glycemic targets, who will wear the devices the majority of the time, in order to improve glycemic control.