Type 1 Diabetes:
Out of the Shadows

Jonathan Weber MA, PA-C, DFAAPA
Yale School of Medicine Physician Associate Program
Yale Medicine, Endocrine & Metabolism Division

May 22, 2022

Yale SCHOOL OF MEDICINE
Physician Associate Program

Faculty

Jonathan Weber, MA, PA-C, DFAAPA

- Assistant Professor & Associate Director of Didactic Education, Section of General Internal Medicine, Yale School of Medicine
  Physician Associate Program, Yale University
  https://medicine.yale.edu/profile/jonathan_weber/

- Yale Medicine, Endocrine & Metabolism Division, Yale Diabetes Center
  https://www.yalemedicine.org/specialists/jonathan_weber

Session Objectives

At the end of the presentation, the participant will be able to:

- ***Compare & contrast the classification & pathophysiology of type 1 & type 2 diabetes***
- ***Review the rationale for a new diagnostic approach for type 1 diabetes***
- ***Explore the proposed ADA/EASD consensus standards of care for patients with type 1 diabetes***
- ***Recognize technological advances in the comprehensive care of patients with type 1 diabetes***
- ***Apply clinical strategies to case-based scenarios for patients with type 1 diabetes***

Pre-Session Questions

1. **What are recommended Time Below Range (TBR) & Time in Range (TIR) blood glucose parameters for patients 18-65 years of age with Type 1 diabetes with no underlying co-morbidities?**

A. > 60% TIR (70-180) & < 4% TBR (<70)
B. > 65% TIR (70-180) & < 4% TBR (<70)
C. > 70% TIR (70-180) & < 4% TBR (<70)
D. > 75% TIR (70-180) & < 4% TBR (<70)

Pre-Session Questions

2. When analyzing the Ambulatory Glucose Profile (AGP) for patients with Type 1 or Type 2 diabetes, the top priority for the clinical encounter is to:

A. Minimize hypoglycemia & improve the A1c
B. Minimize hyperglycemia & improve the A1c
C. Minimize hypoglycemia & maintain glucose variability
D. Minimize hypoglycemia & reduce glucose variability

Pre-Session Questions

3. The initial diagnostic measure(s) for suspected T1DM proposed by the ADA/EASD in July 2021 include (s):

A. C-peptide
B. GAD antibody
C. C-peptide & GAD antibody
D. GAD antibody & Zinc transporter antibody

26-year-old presents for follow-up appointment…

- **HPI – Patient was seen initially 1 week ago for symptoms of new onset excessive thirst & increased urinary frequency.**
- **Previously healthy without other PMH or contributory Social Hx. Family Hx is significant for DM – both Type 1 DM (father & paternal aunt) & Type 2 DM (paternal uncles x 2).**
- **The patient expresses concerns about how possibility of diabetes might impact his/her life.**
- **Patient was advised to obtain routine work & to f/u in 1 week.**

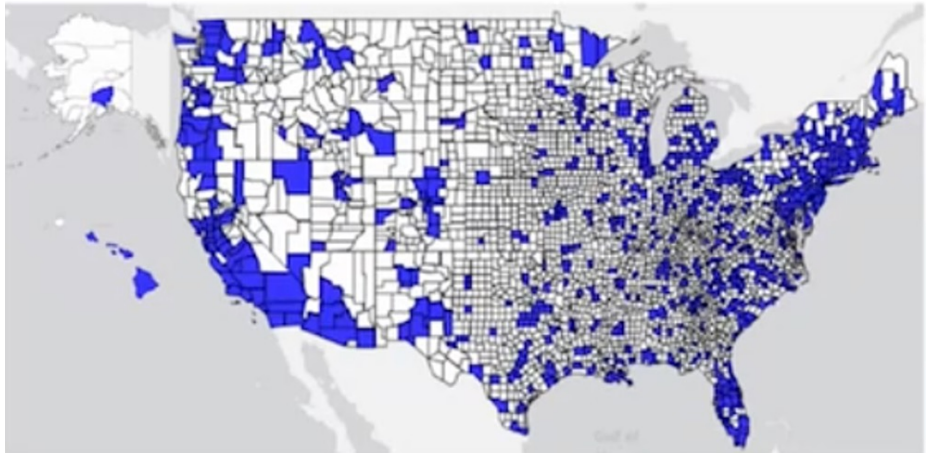
Disclosures

- **I have no relevant relationships with ineligible companies to disclose within the past 24 months.**
- **Moonlight as pancreas 24/7/365 x 33 years**

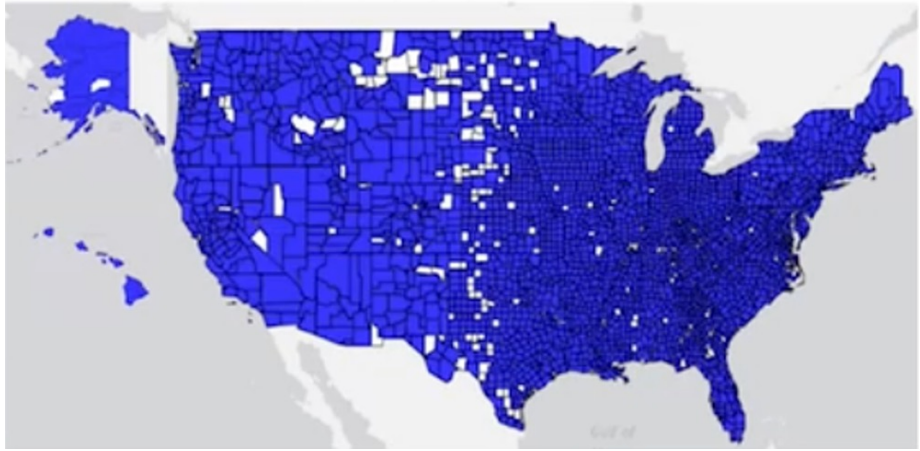
Patient Perspective ⟷ *Provider Perspective*

Distribution of Endocrinologists/Diabetologists & PCPs in US[1]

US Counties with ≥ 1
Pediatric or Adult Endocrinologist/Diabetologist



US Counties with ≥ 1
Primary Care Provider



Total PCPs in the US[2]:

PAs: 20%

NPs: 30%

MD/DOs: 50%

[1]Oser SM, Oser TK. Diabetes Technologies: We Are All in This Together. Clin Diabetes. 2020 Apr;38(2):188-189. doi: 10.2337/cd19-0046. PMID: 32327892; PMCID: PMC7164996.
[2]Petterson S, McNellis R, Klink K, Meyers D, Bazemore A. The State of Primary Care in the United States: A Chartbook of Facts and Statistics. January 2018.

General Classification Categories for Diabetes

Type 1 diabetes

- Autoimmune ß-cell destruction, usually leads to insulin deficiency, including latent autoimmune diabetes of adulthood (LADA)

~5%

Type 2 diabetes

- Progressive loss of ß-cell mass & insulin secretion frequently on background of insulin resistance

90-95%

Specific types of diabetes due to other causes

- Monogenic syndromes (neonatal & maturity-onset diabetes of young [MODY])
- Diseases of exocrine pancreas (cystic fibrosis & pancreatitis)
- Drug-induced diabetes (steroid-induced in patients with HIV s/p organ transplant)

<1%

Gestational diabetes mellitus

- Diagnosed in 2nd or 3rd trimester & not clearly overt diabetes prior to gestation

6-9%

Classification and Diagnosis of Diabetes: *Standards of Medical Care in Diabetes - 2022. Diabetes Care* 2022;45(Suppl. 1):S17-S38

Foundations of T1DM - Islets of Langerhans

Courtesy of Silvio Inzucchi, Yale Endocrinology & Metabolism

History of Type 1 Diabetes & Insulin

- Before early 1920's, Type 1 diabetes was a death sentence
  - Most common treatment was a starvation diet
  - Treatment led to skyrocketing glucose levels, DKA & death

- In early 1920's, Banting & Best
  - Successes with dog insulin
  - 1st human received dog insulin
  - "Miracle" substance called "insulin" from Latin *insula*, meaning "island"

- Eli Lilly & Company - 1923
  - Mass-production of insulin (derived from pancreases of pigs & cows)
  - For the first time, diabetes was not a death sentence

100 years ago

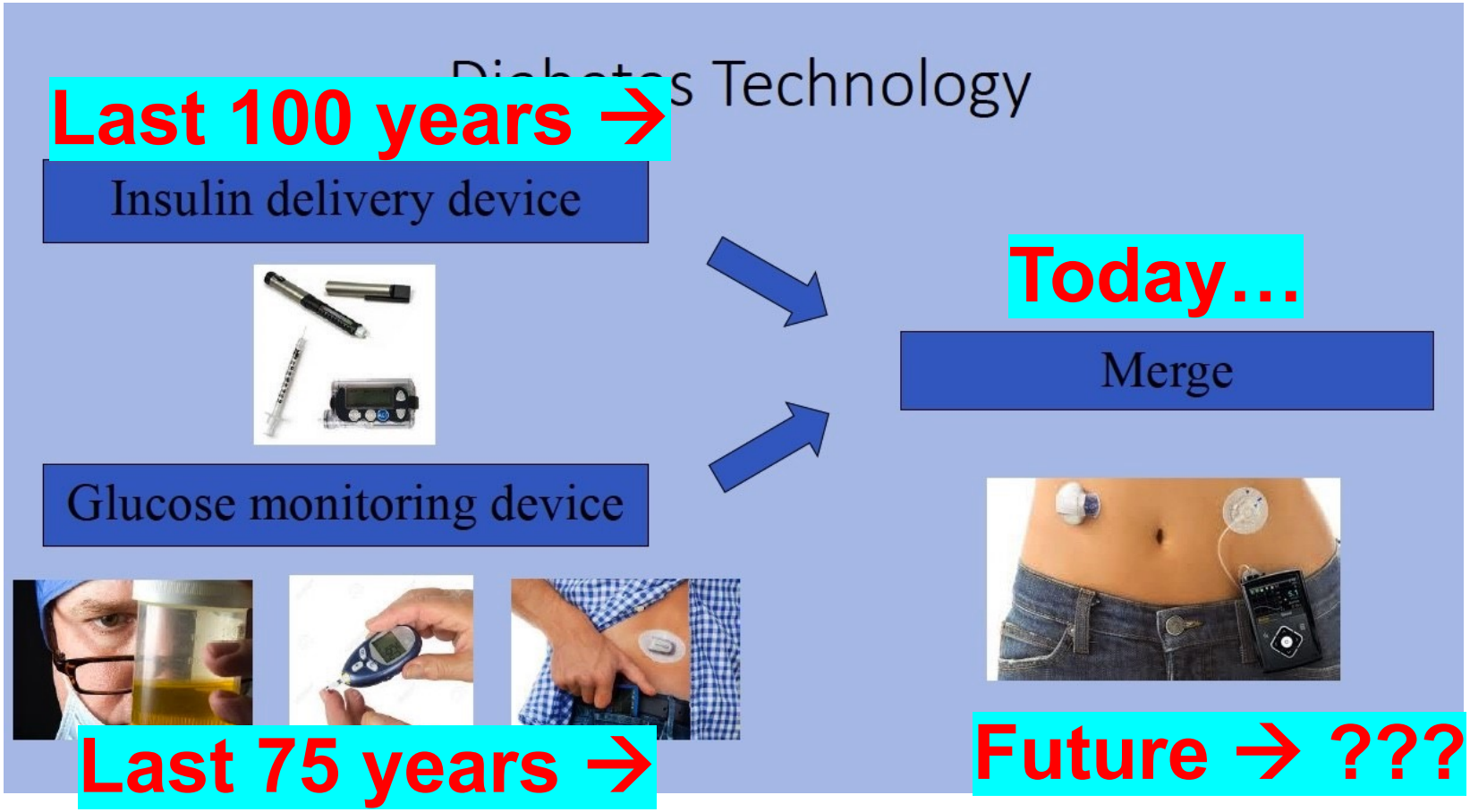
History of Insulin & JW's Type 1 DM Family Tree

William Frederick Weber, 26
(T1DM 1922)

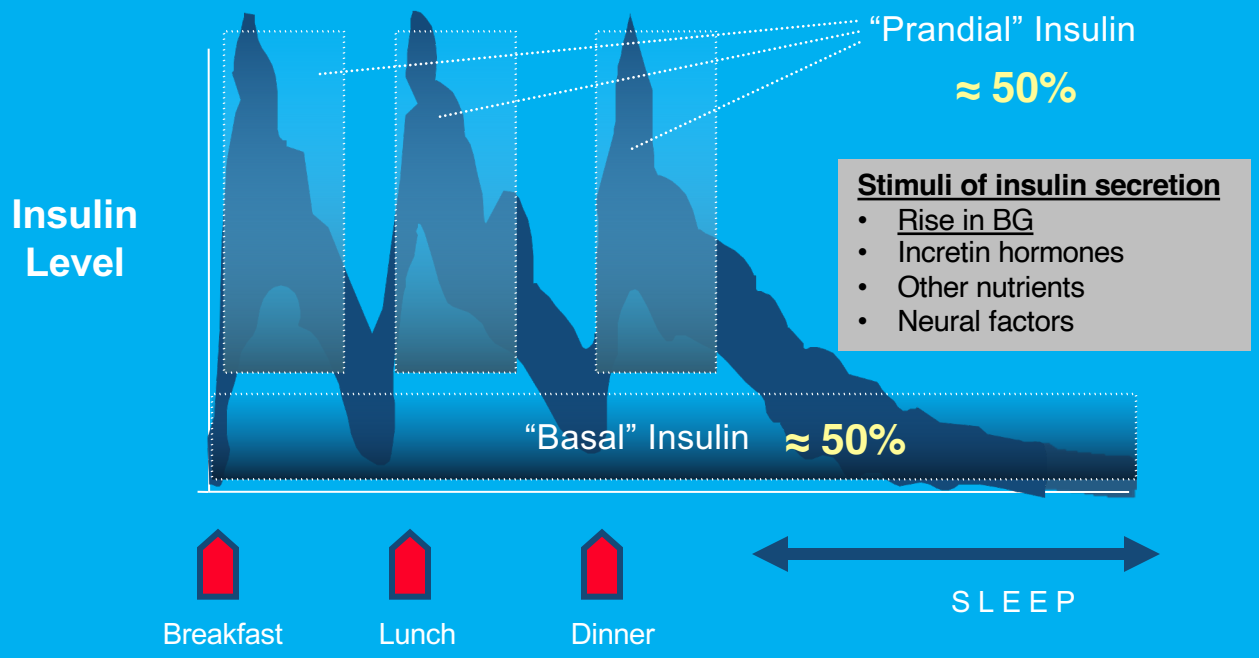
William Walter Weber, 26
(T1DM 1957)

Jonathan Merritt Weber, 26
(T1DM 1989)

History of Type 1 Diabetes Care & Tech Integration

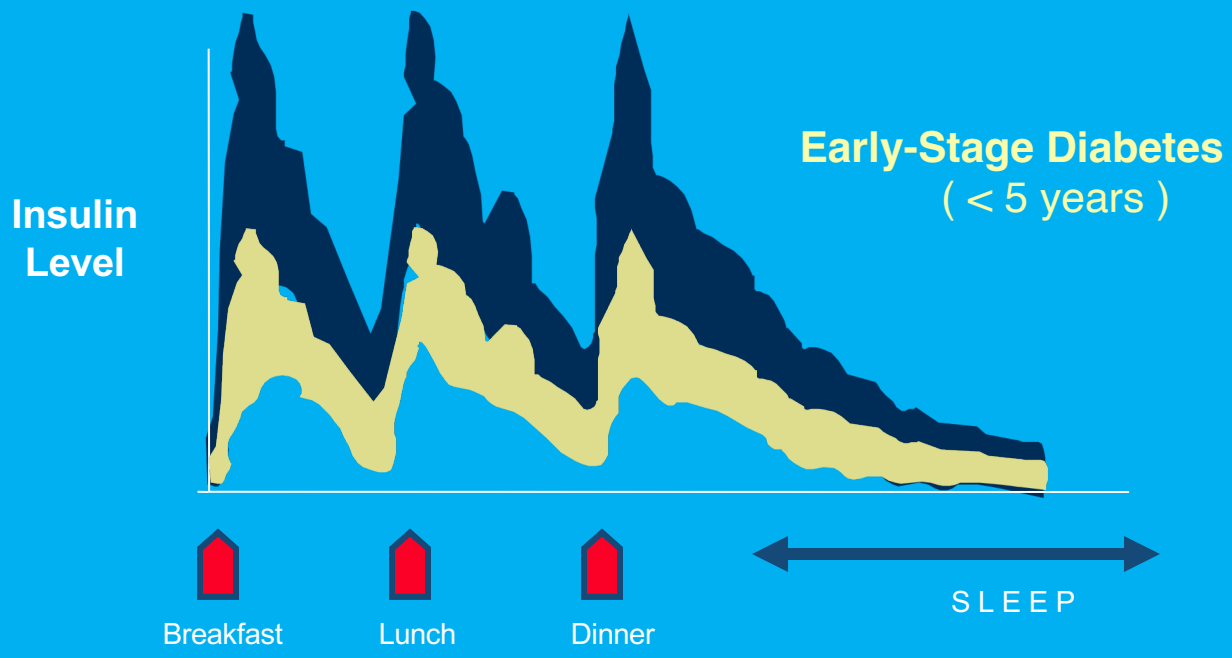


Normal Secretory Pattern of Insulin



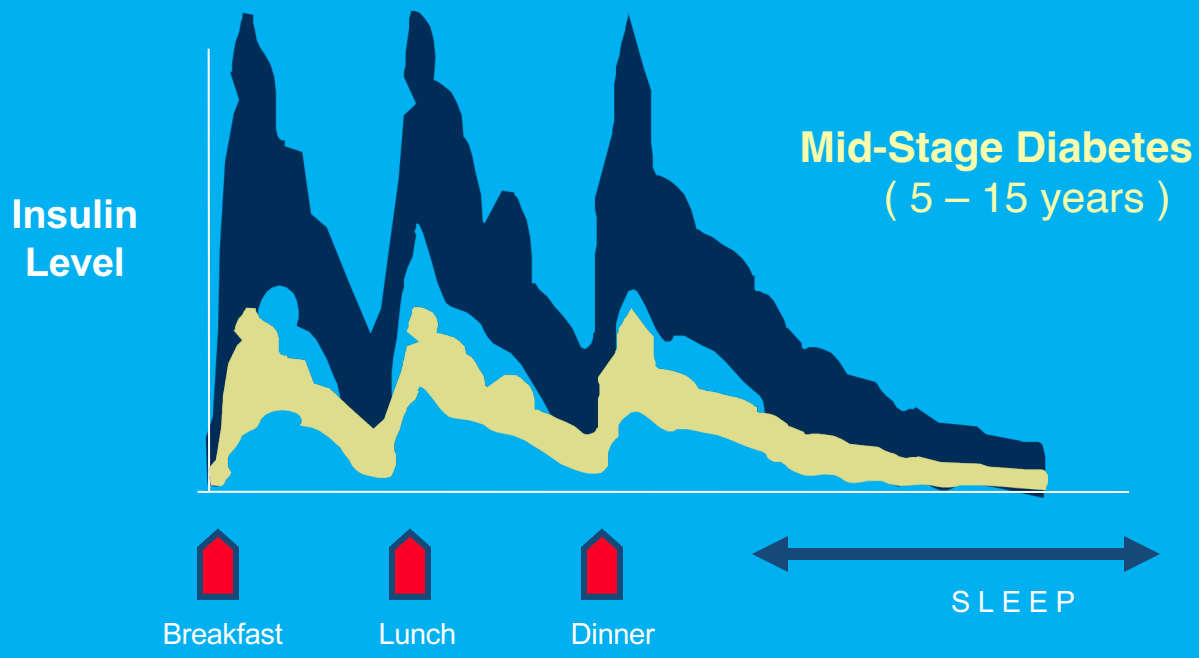
Courtesy of Silvio Inzucchi, Yale Endocrinology & Metabolism

Abnormal Insulin Secretion in T2DM



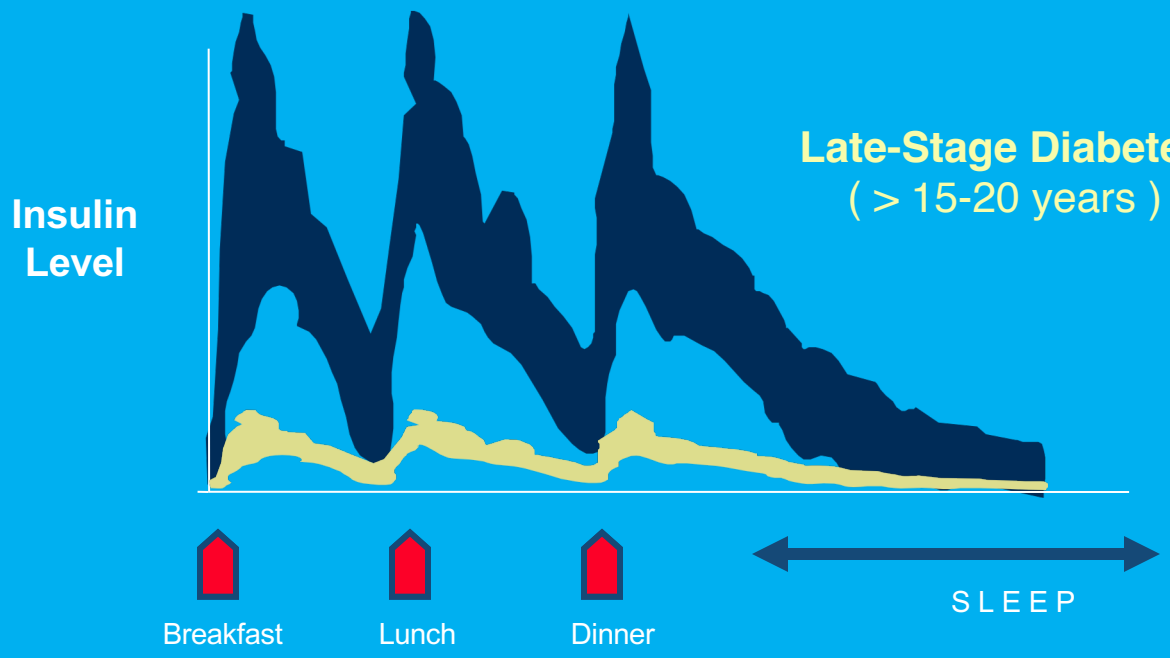
Courtesy of Silvio Inzucchi, Yale Endocrinology & Metabolism

Abnormal Insulin Secretion in T2DM



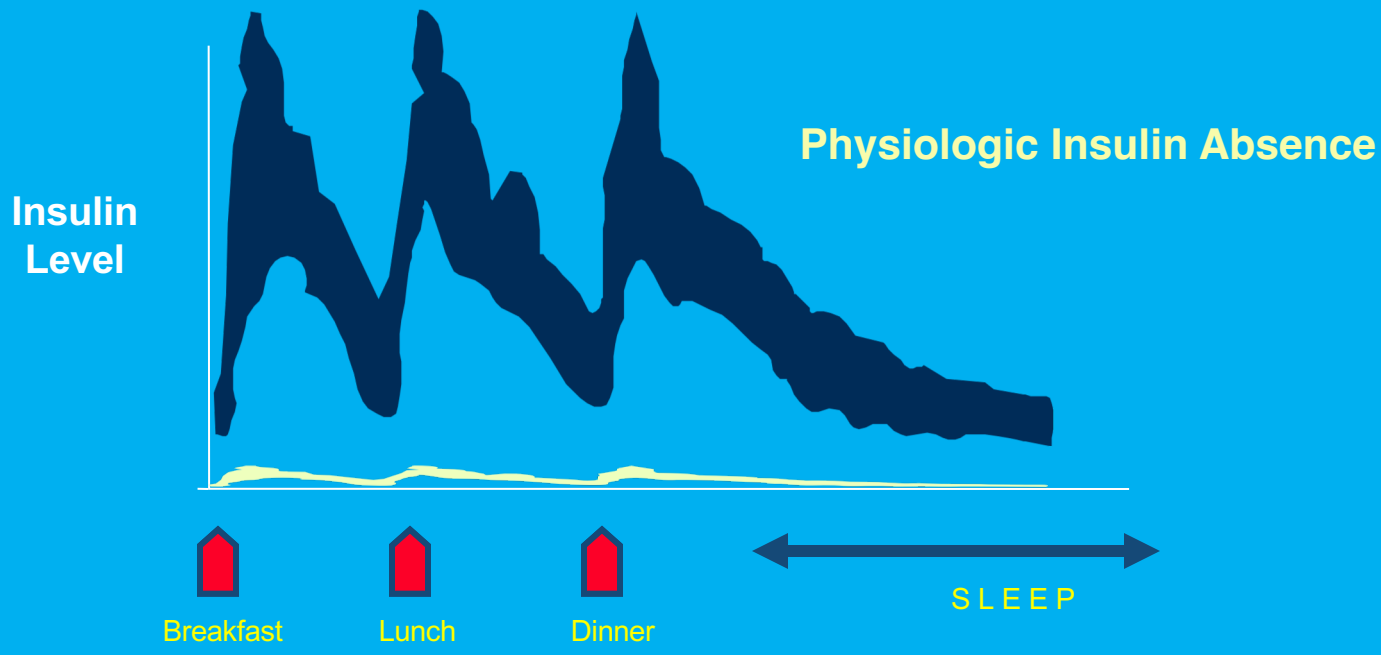
Courtesy of Silvio Inzucchi, Yale Endocrinology & Metabolism

Abnormal Insulin Secretion in T2DM



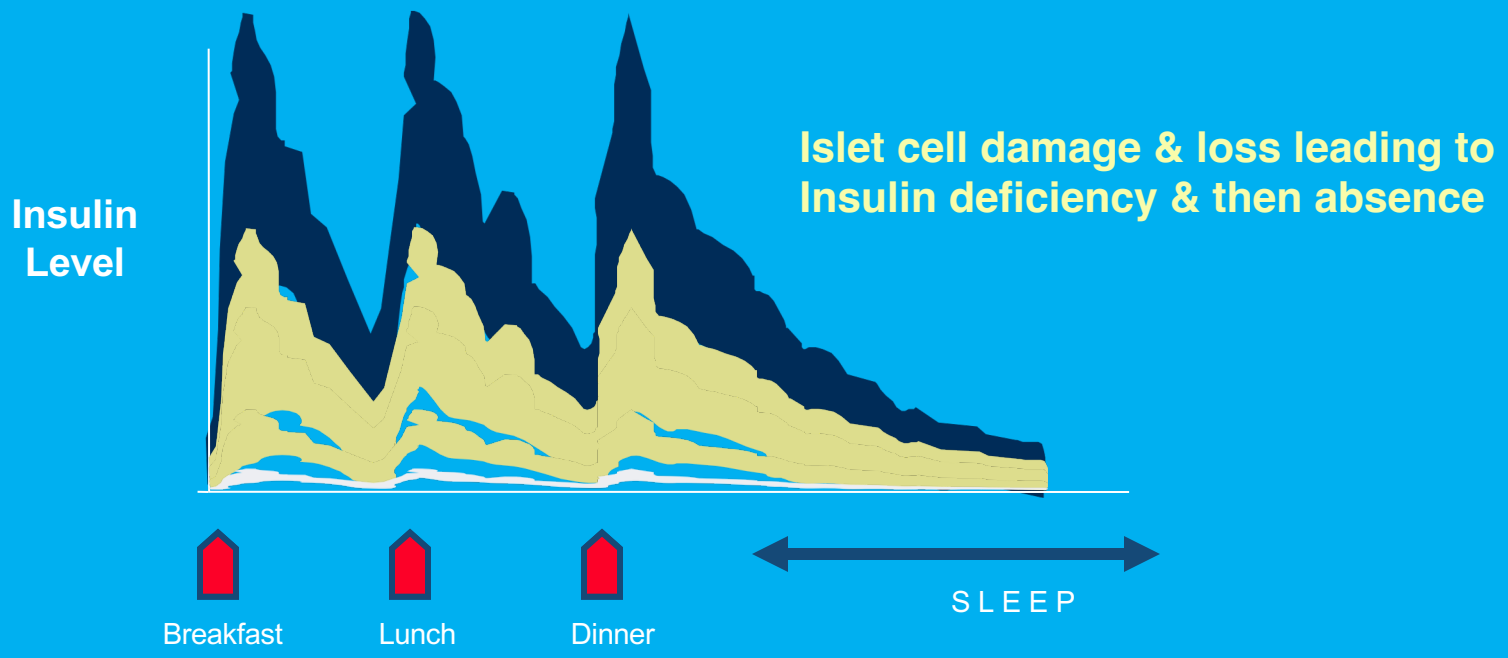
Courtesy of Silvio Inzucchi, Yale Endocrinology & Metabolism

Absent Insulin Secretion in T1DM



Courtesy of Silvio Inzucchi, Yale Endocrinology & Metabolism

Honeymoon Period of Type 1 Diabetes



Clinical Features of Distinguishing Diabetes Types

Clinical features	Type 1 DM	Type 2 DM	Monogenic diabetes
Age of diagnosis	Majority <25, but can occur at any age	Typically > 25 but incidence increasing in adolescents	<25
Weight	Usually lean/thin; higher weight patients becoming more common	>90% at least overweight	Similar to general population
Autoantibodies	Present	Absent	Absent
Insulin dependent	Yes	No	No
Insulin sensitivity	Normal when controlled	Decreased	Normal (may be decreased if obese)
FamHx of diabetes	Infrequent (5-10%)	Frequent (75-90%)	Multigenerational, ie, ≥3 generations
Risk of DKA	High	Low	Low

Data from: Naylor R et al. Clin Endocrinol (Oxf) 2011; 75:422; Ramesh SC, et al. Indian J Pediatr 2012; 79:955; Thanabalasingham G et al. BMJ 2011; 343:d6044; Pinhas-Hamiel O et al. J Pediatr 2005; 146:693; De Ferranti SD et al. Diab Vasc Dis Res 2007; 4:285.

ADA Classification & Diagnosis of Type 1 Diabetes

Table 2.1—Staging of type 1 diabetes (12,15)

	Stage 1	Stage 2	Stage 3
Characteristics	• Autoimmunity • Normoglycemia • Presymptomatic	• Autoimmunity • Dysglycemia • Presymptomatic	• Autoimmunity • Overt hyperglycemia • Symptomatic
Diagnostic criteria	• Multiple islet autoantibodies • No IGT or IFG	• Islet autoantibodies (usually multiple) • Dysglycemia: IFG and/or IGT • FPG 100–125 mg/dL (5.6–6.9 mmol/L) • 2-h PG 140–199 mg/dL (7.8–11.0 mmol/L) • A1C 5.7–6.4% (39–47 mmol/mol) or ≥10% increase in A1C	• Autoantibodies may become absent • Diabetes by standard criteria

FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; 2-h PG, 2-h plasma glucose.

Classification and Diagnosis of Diabetes: *Standards of Medical Care in Diabetes - 2022*. *Diabetes Care* 2022;45(Suppl. 1):S17-S38

Goals of ADA/EASD Consensus Statement on T1DM

Diagnosis of T1DM

Differentiating T1DM from T2DM

Differentiating T1DM from monogenic diabetes

Investigating adults with suspected T1DM

Holt RIG et al. The management of type 1 diabetes in adults. A consensus report by the ADA & EASD. (Draft) ADA's 2021 Scientific Sessions.

Diagnosis of Type 1 DM in Adults

Clinical Presentation:

- Short duration illness of 1–4 weeks or a slowly evolving process
- Can be mistaken for type 2 diabetes
- Classic triad: thirst/polydipsia, polyuria & weight loss

Hallmarks & Exceptions of T1DM:

- Profound insulin deficiency is typical hallmark of T1DM
- Some maintain insulin secretion for years after diagnosis & may not require insulin treatment at diagnosis

Holt RIG et al. The management of type 1 diabetes in adults. A consensus report by the ADA & EASD. (Draft) ADA's 2021 Scientific Sessions.

Differentiating Type 1 DM & Type 2 in Adults

Most discriminative clinical features of T1DM:

- Younger age at diagnosis (<35 years) & lower BMI (<25 kg/m2)
- Glucose >360 mg/dL (20 mmol/L)
- Unintentional weight loss
- Ketoacidosis

Most discriminative clinical features of T2DM:

- Overweight or obesity
- Less marked hyperglycemia
- Absence of weight loss
- Absence of ketoacidosis

Clinical Considerations:

- No single clinical feature confirms T1DM in isolation
- Rapid progression to insulin (< 3 years) strongly suggestive of T1DM at any age

Holt RIG et al. The management of type 1 diabetes in adults. A consensus report by the ADA & EASD. (Draft) ADA's 2021 Scientific Sessions.

Investigation of Suspected Type 1 DM in Adults

Primary diagnostic measures for suspected T1DM:

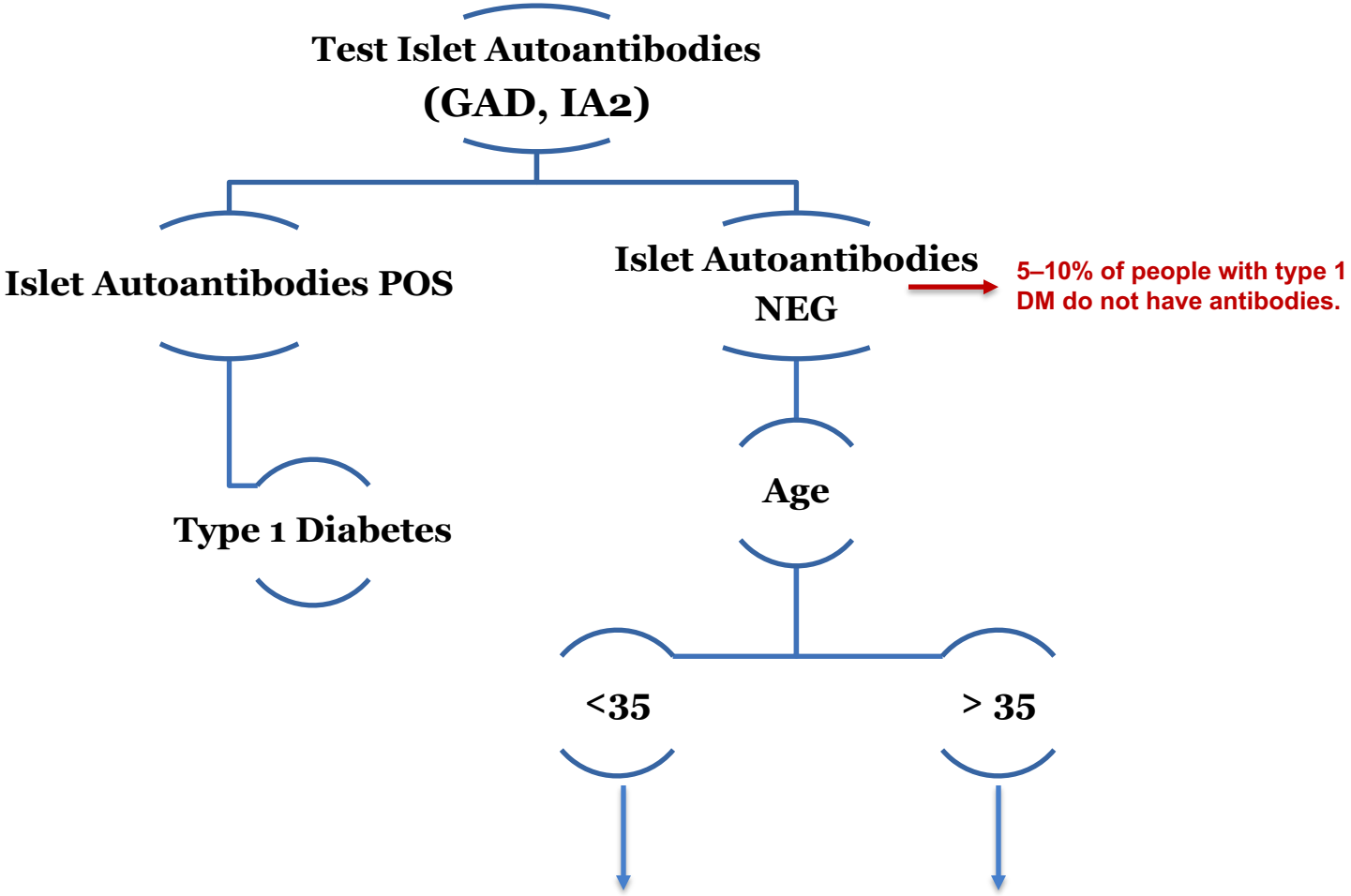
- Presence of Glutamic Acid Decarboxylase (GAD 65) antibody
- If GAD Ab NEG, then check Islet tyrosine phosphatase 2 (IA2) & Zinc transporter 8 (ZNT8)
- Presence of $\geq$ 1 positive autoantibodies is highly predictive of rapid progression of severe insulin deficiency & T1DM

Considerations & Clinical Judgement:

- 5-10% of patients with T1DM do not have antibodies
- If clinically suspicious of T1DM, the patient should be treated with insulin regardless of antibody lack or features of T2DM

Holt RIG et al. The management of type 1 diabetes in adults. A consensus report by the ADA & EASD. (Draft) ADA's 2021 Scientific Sessions.

Flowchart Investigation: Adult with Suspected Type 1 DM

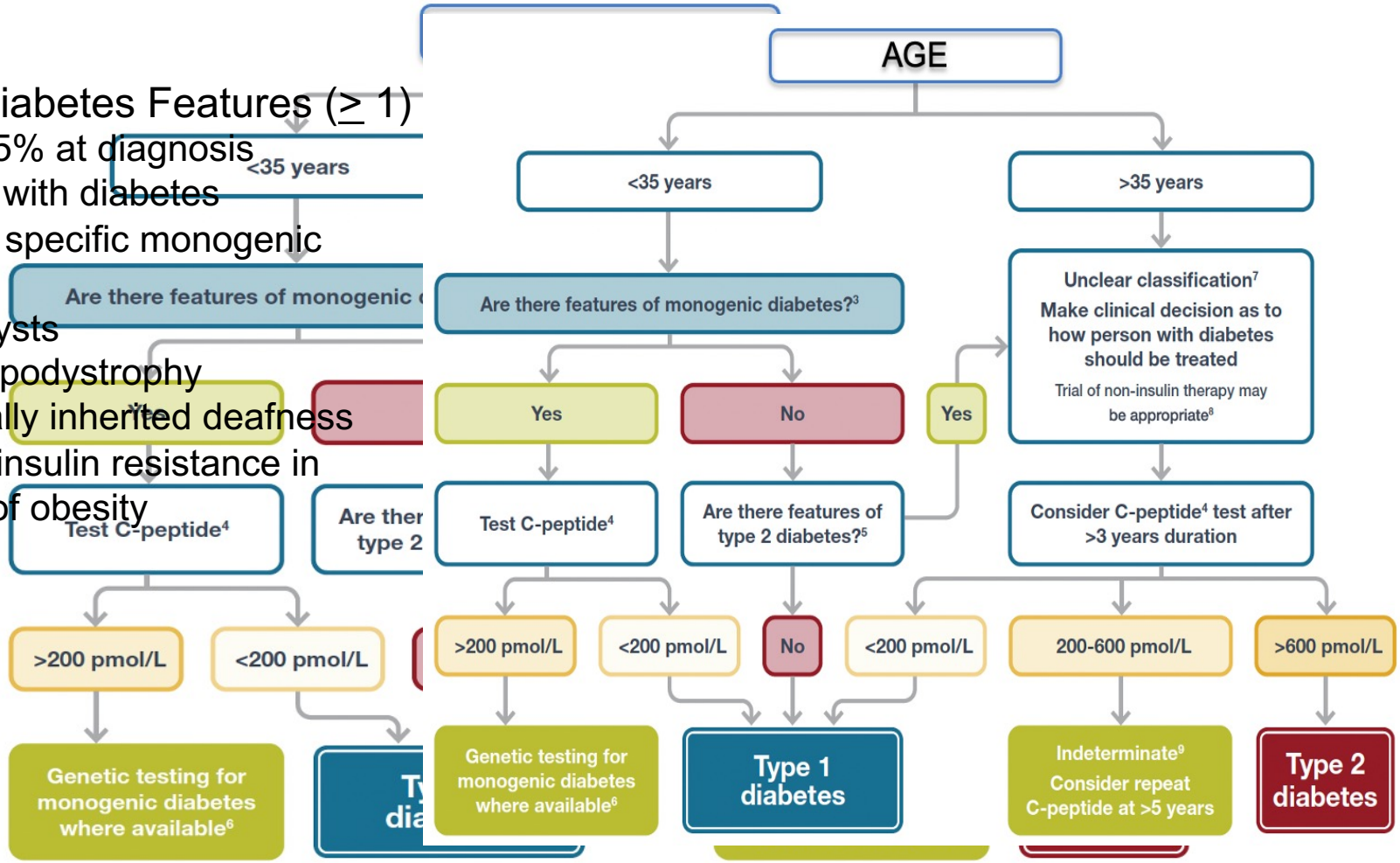


Adapted from: Holt RIG et al. The management of type 1 diabetes in adults. A consensus report by the ADA & EASD. (Draft) ADA's 2021 Scientific Sessions.

Flowchart Investigation: Adult with Suspected Type 1 DM

Monogenic Diabetes Features (≥ 1)

- HbA1c < 7.5% at diagnosis
- One parent with diabetes
- Features of specific monogenic cause:
  - ➢Renal cysts
  - ➢Partial lipodystrophy
  - ➢Maternally inherited deafness
  - ➢Severe insulin resistance in absence of obesity



Adapted from: Holt RIG et al. The management of type 1 diabetes in adults. A consensus report by the ADA & EASD. (Draft) ADA's 2021 Scientific Sessions.

What about the C-Peptide in suspected T1DM?

When to obtain a C-peptide?

- **Check C-peptide only if T1DM diagnosis uncertain after 3 years**
- Only indicated in patients with diabetes receiving insulin treatment

Interpretation of C-peptide

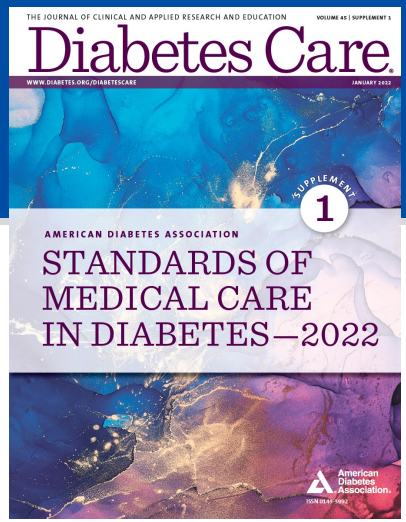
- Low levels indicate pancreas is producing little to no insulin
- Low to no C-peptide is usually consistent with T1DM
- A low level may be normal if you have not eaten within 5 hours of test

Clinical Considerations

- **11% of patients clinically diagnosed with T1DM were reclassified after routine C-peptide testing > 3 years**

Holt RIG et al. The management of type 1 diabetes in adults. A consensus report by the ADA & EASD. (Draft) ADA's 2021 Scientific Sessions.

Proactive Management of Diabetes



Diagnosis

Lifestyle modification & Diabetes Self-Management Education & Support (DSMES)

Glucose Control

Improve glycemic control to reduce symptoms & microvascular risk

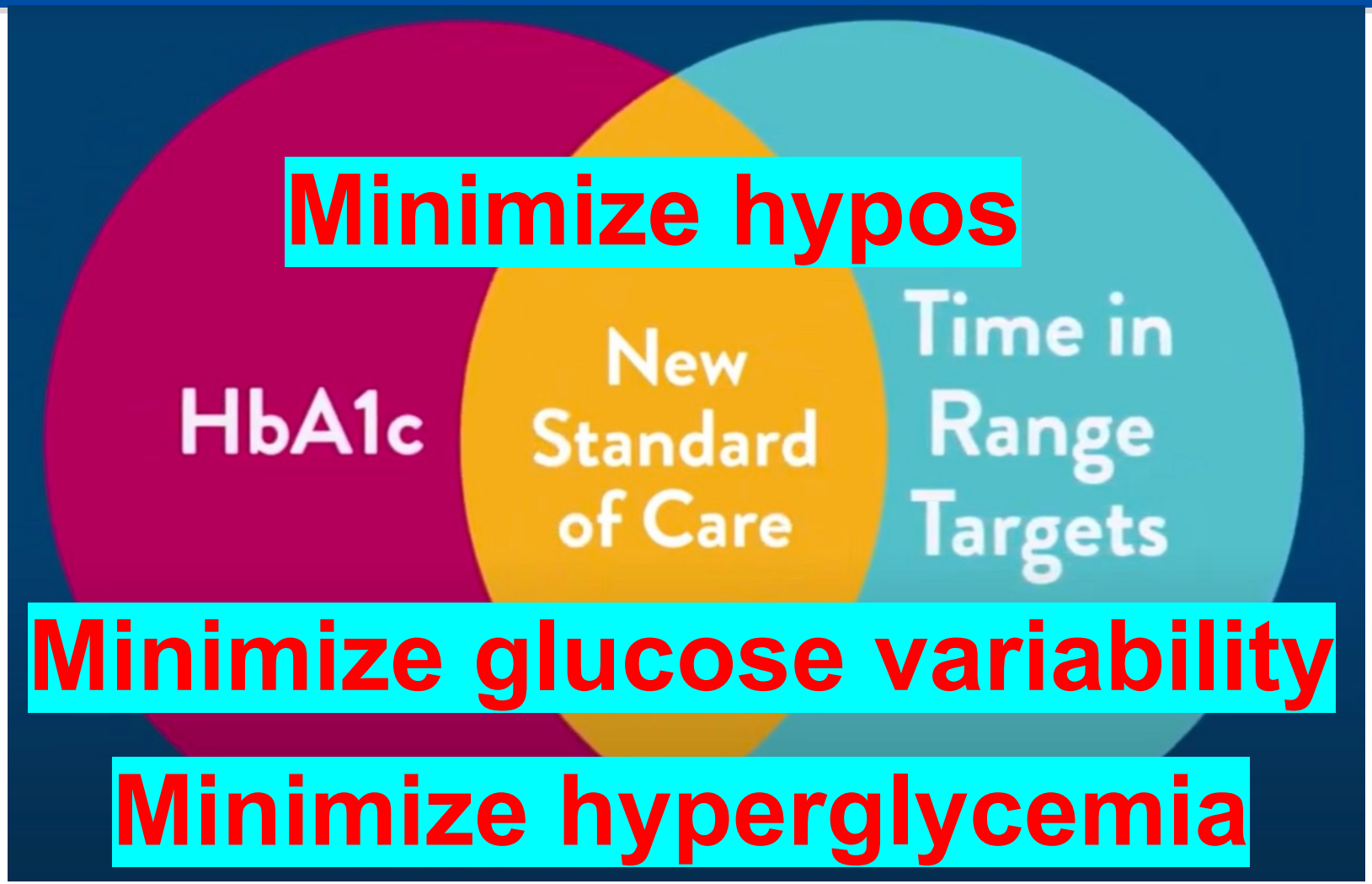
Cardiovascular Risk

Reduce macrovascular risk especially by controlling lipids & blood pressure

Comorbidities

Manage co-morbidities (obesity, CVD, CKD, depression, fatty liver, eye & neuropathic disease)

New Standards of Care

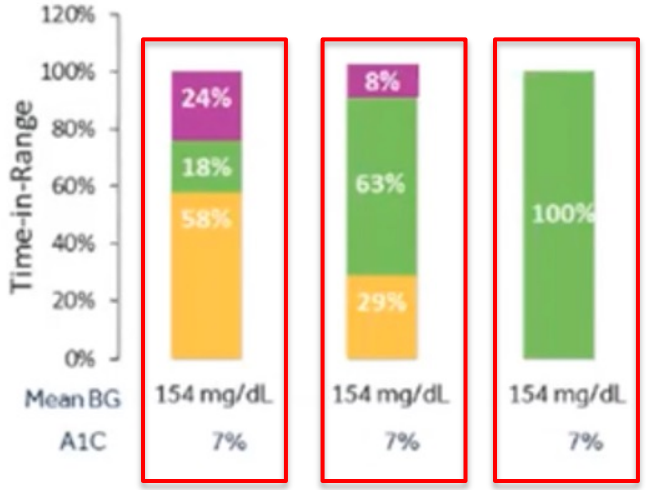


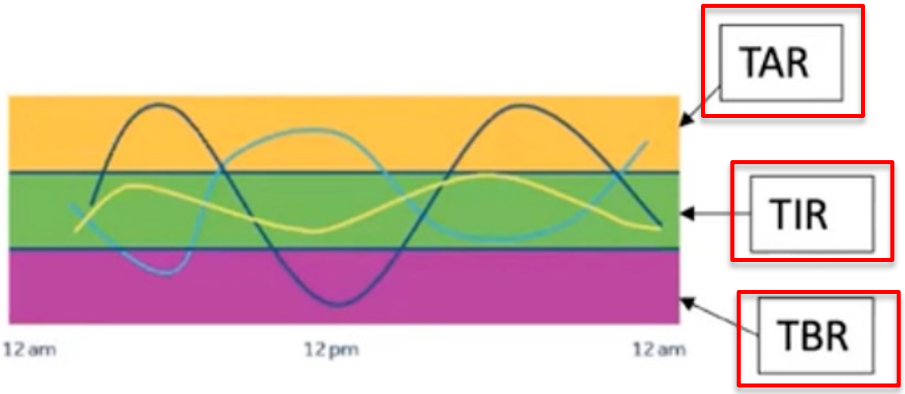
Limitations of Hemoglobin A1c

- Unable to reflect acute glycemic excursions
- A1c may be inaccurate in a range of physiologic and pathologic conditions
- Does not provide time-specific blood glucose data

Ambulatory Glucose Profile →

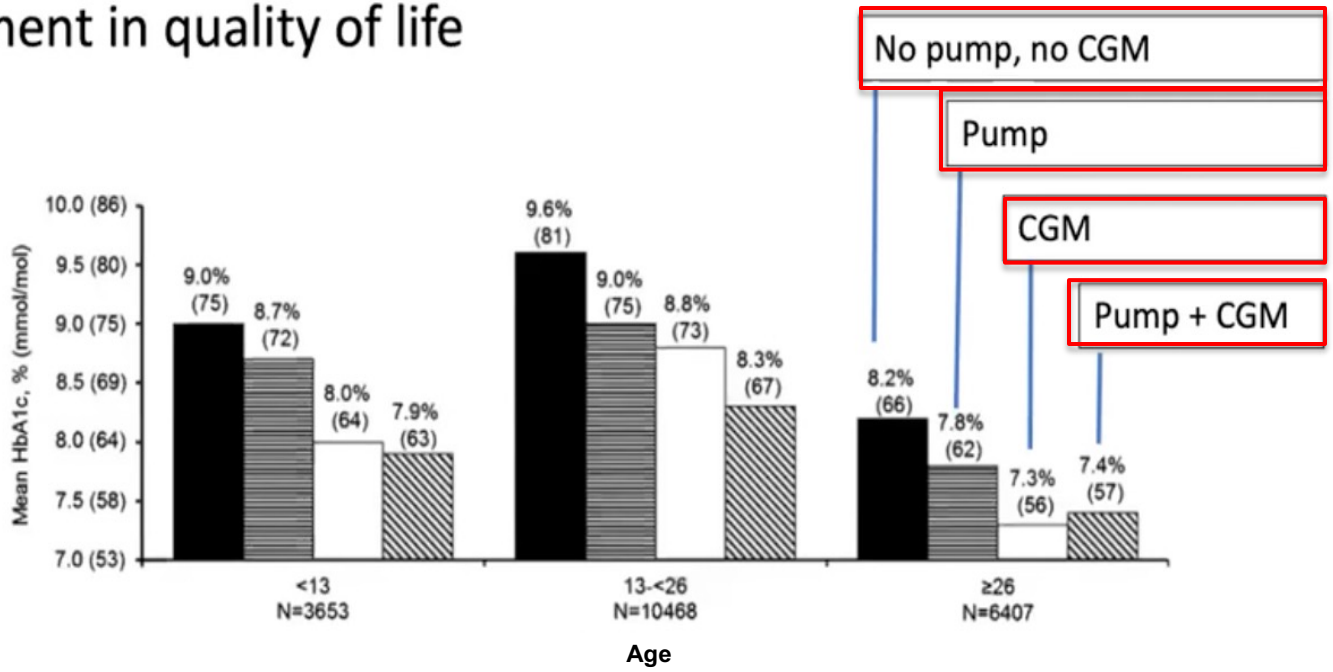
7-14-30 day profile of BG trends





Why Use Technology?

- Improved glycemic control
- Reduction in hypoglycemia
- More information on daily fluctuations
- Potential improvement in quality of life



Foster et al. Diabetes Tech. Ther. 2019, DOI: 10.1089/dia.2018.0384

Glycemic Targets for Patients with Diabetes[1,2]

Patient Characteristics	Reasonable HbA_{1c} Goal, %	Recommended Blood Glucose % for TIR or TBR
Nonpregnant adults aged <65 years with type 1 or 2 diabetes	<7.0	>70% of TIR 70-180 mg/dL <4% of TBR ≤69 mg/dL
Healthy adults aged ≥65 years with diabetes and few coexisting chronic illnesses	7.0-7.5	Fasting preprandial goal: 80-130 mg/dL Peak postprandial: <180 mg/dL
Adults aged ≥65 years with diabetes and multiple coexisting chronic illnesses	<8.0	>50% of TIR 70-180 mg/dL <1% of TBR ≤69 mg/dL

TBR, time below range; **TIR**, time in range

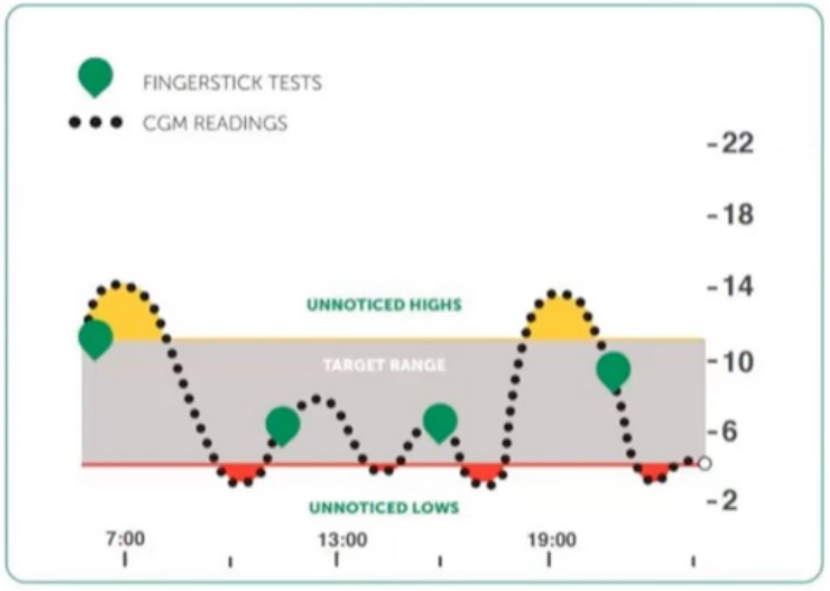
[1]ADA.Glycemic Targets. *Diabetes Care.* 2022;45(Suppl.1):S83-S96.
[2]Battelino T, Danne T, Bergenstal RM, et al. *Diabetes Care*. 2019;42(8):1593-1603. doi:10.2337/dci19-0028

Continuous Glucose Monitoring (CGM)

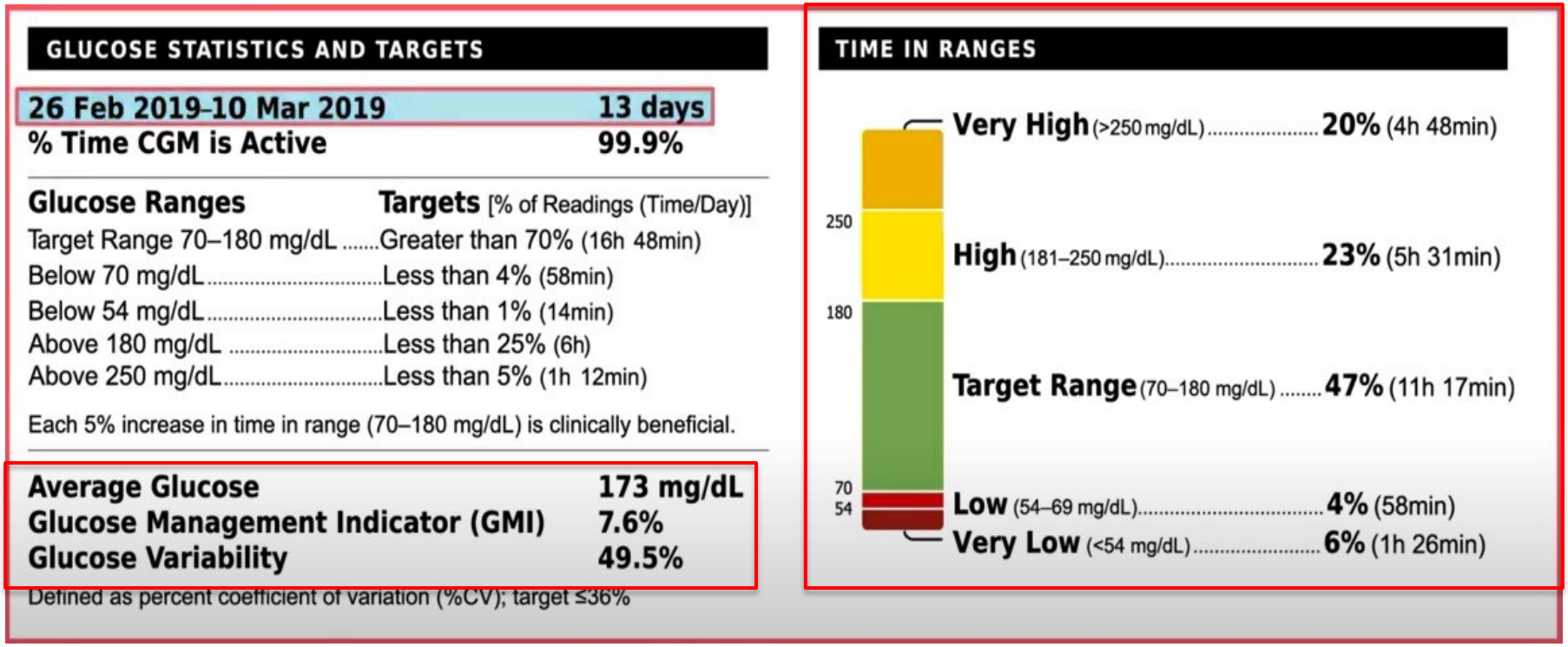
- Subcutaneous glucose sensor → transmitter → display
- Measures glucose levels every 5 minutes
- PROFESSIONAL DEVICES
  - Owned by clinic
  - Retrospective or Real-Time

- PERSONAL DEVICES:
  - Intermittently scanned or real-time

Ambulatory Glucose Profile



CGM Ambulatory Glucose Profile (AGP) Report



GLUCOSE STATISTICS AND TARGETS

26 Feb 2019–10 Mar 2019	**13 days**
% Time CGM is Active	**99.9%**

Glucose Ranges	**Targets** [% of Readings (Time/Day)]
Target Range 70–180 mg/dL	Greater than 70% (16h 48min)
Below 70 mg/dL	Less than 4% (58min)
Below 54 mg/dL	Less than 1% (14min)
Above 180 mg/dL	Less than 25% (6h)
Above 250 mg/dL	Less than 5% (1h 12min)

Each 5% increase in time in range (70–180 mg/dL) is clinically beneficial.

Average Glucose	**173 mg/dL**
Glucose Management Indicator (GMI)	**7.6%**
Glucose Variability	**49.5%**

Defined as percent coefficient of variation (%CV); target ≤36%

TIME IN RANGES

250
180
70
54

Very High (>250 mg/dL) **20%** (4h 48min)

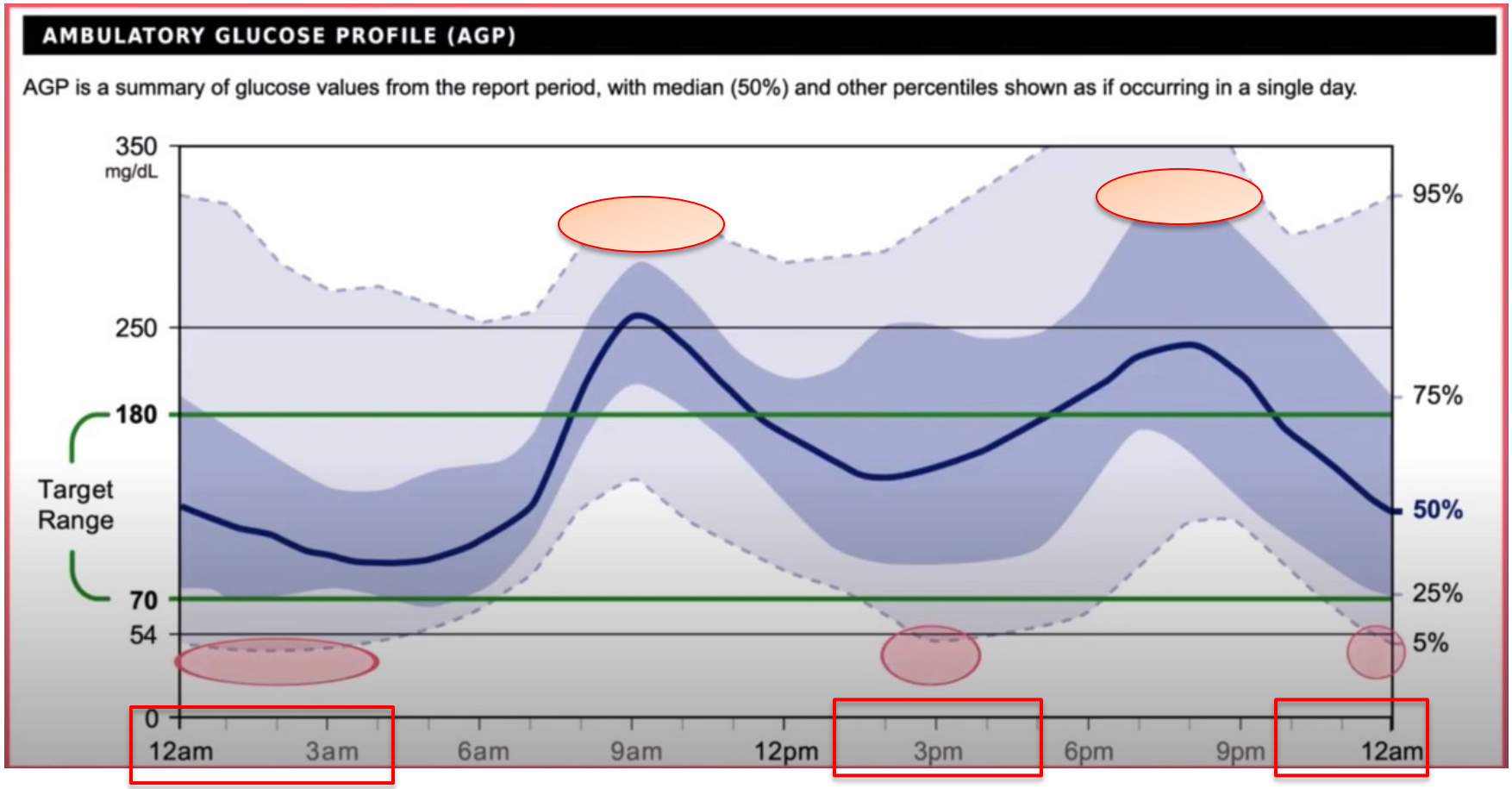
High (181–250 mg/dL) **23%** (5h 31min)

Target Range (70–180 mg/dL) **47%** (11h 17min)

Low (54–69 mg/dL) **4%** (58min)

Very Low (<54 mg/dL) **6%** (1h 26min)

Ambulatory Glucose Profiles (AGPs)



Systematic Approach to Patients' BGM/CGM reports

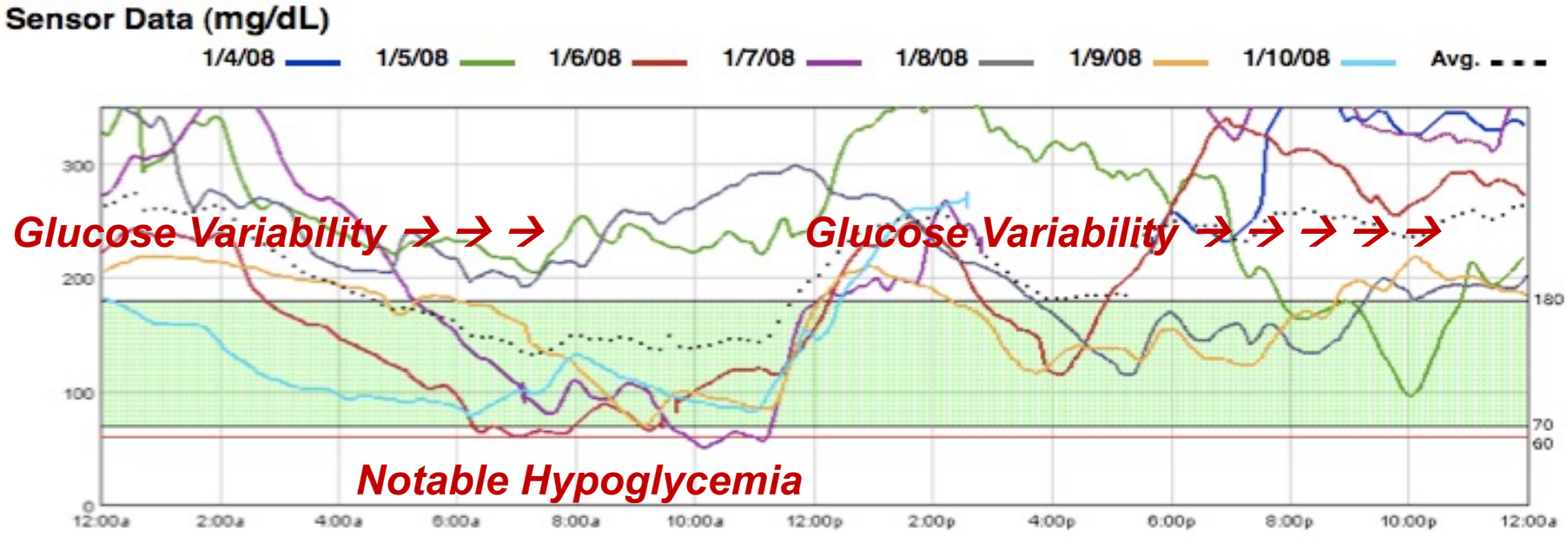
Minimize

- Hypoglycemia
- Glucose variability
- Hyperglycemia

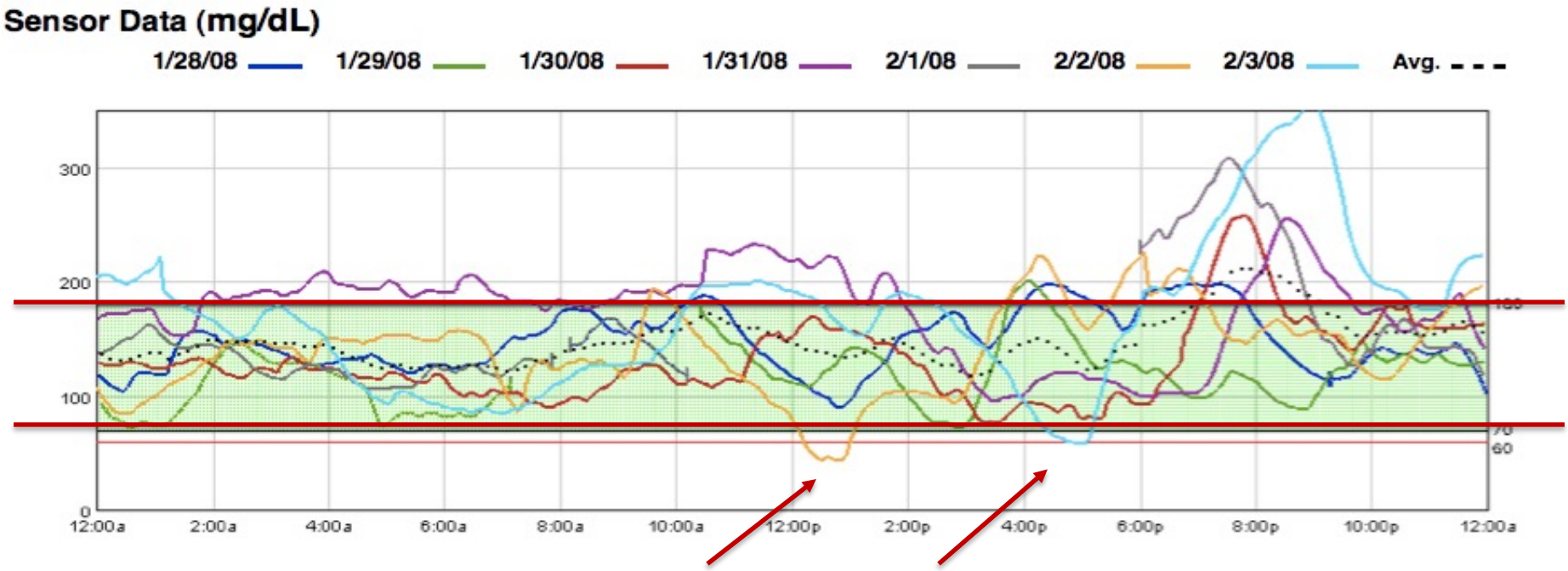
Priorities

- Reduce hypoglycemia (TBR)
- Increase Time in Range (TIR)

CGM Tracing of Patient with T1DM



Follow-up CGM Tracing after Insulin Adjustments



Insulin's Key Features

- Remains most powerful & versatile tool to control blood glucose.
- Dosing potential & A1C reduction is only limited by risk of hypoglycemia.
- Patients with type 1 diabetes are at greater risk for hypoglycemia than patients with type 2 diabetes.
- Significant increase in types & varieties of insulin products over the past 10-15 years

Pharmacokinetics of Insulin Products

Insulin Preparation	Onset	Peak	Duration
	TRADE NAMES		
Inhaled human insulin	**Afrezza**		
Lispro, Aspart, Glulisine	**Humalog U-100, -200, Lyumjev, Novolog, Fiasp, Apidra**		
Human Regular	**Humulin-R, Novolin-R, ReliOn-R**		
Human NPH	**Humulin-N, Novolin-N ReliOn-N**		
Glargine, Detemir, Degludec	**Lantus, Basaglar, Levemir, Toujeo, Tresiba U-100, -200**		

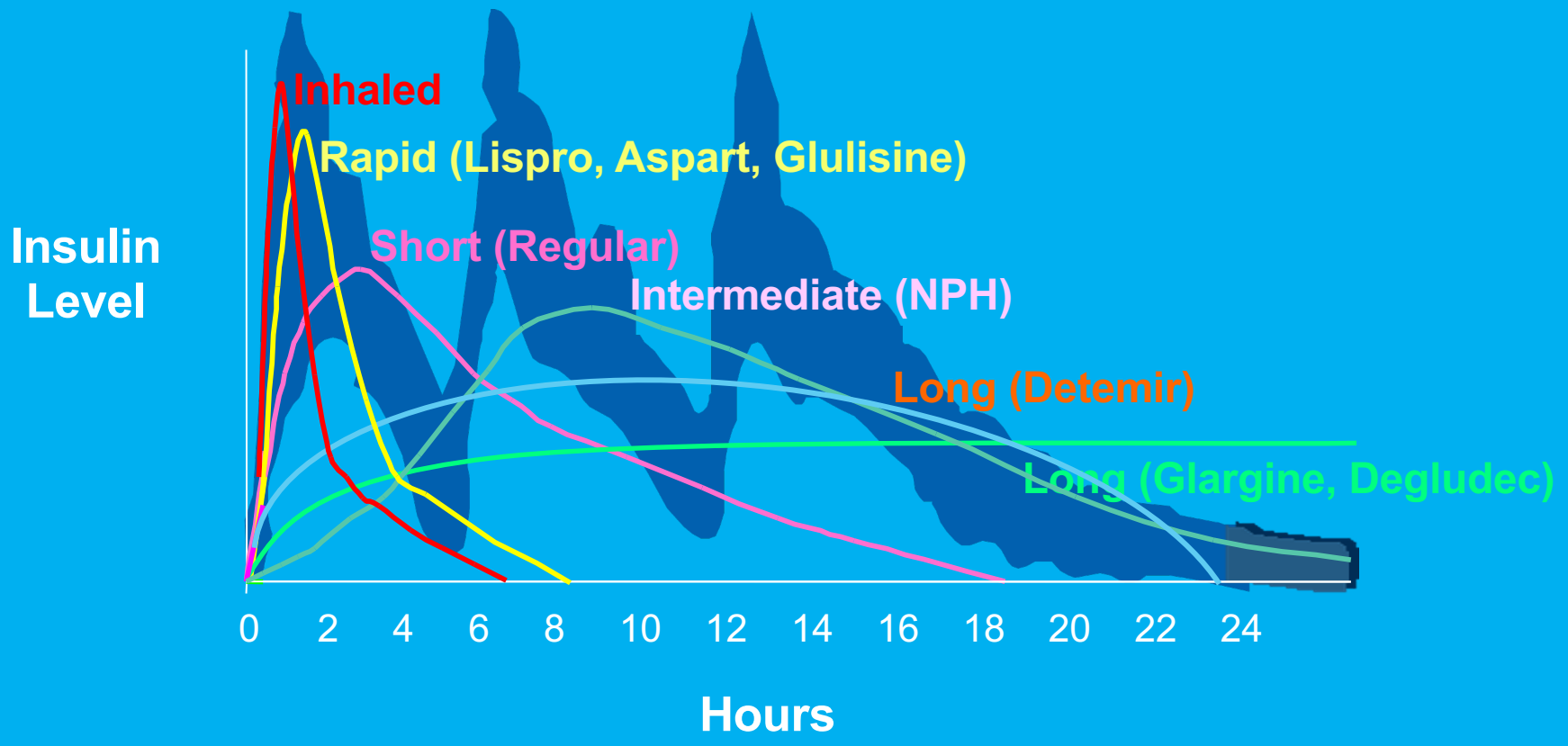
Humalog 75/25, 50/50
Novolog 70/30

Humulin 70/30
Novolin 70/30
ReliOn 70/30

The time course of action of any insulin may vary in different individuals, or at different times or different injection locations in the same individual. Due to such variation, the time periods described above should be used as general guidelines only.

Courtesy of Silvio Inzucchi, Yale Endocrinology & Metabolism

Pharmacokinetics of Insulin Formulations

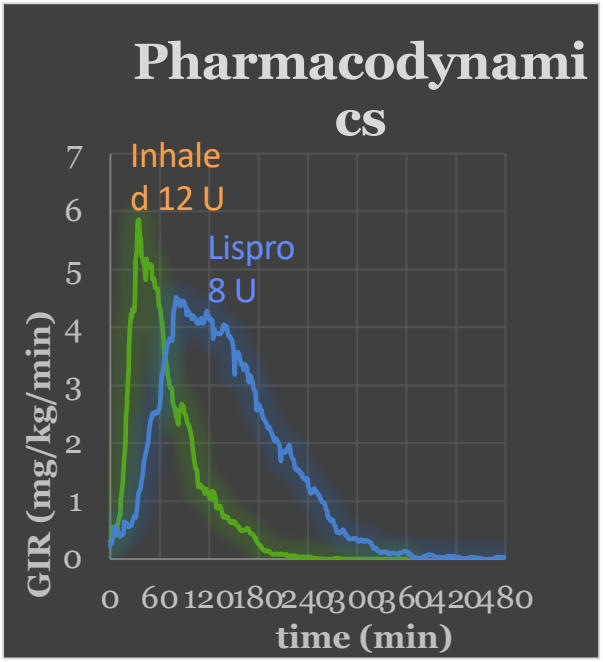


Courtesy of Silvio Inzucchi, Yale Endocrinology & Metabolism

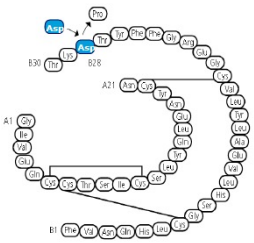
Ultra-Rapid Insulins: Examples

Inhaled insulin

-2X appearance in blood stream
-2X higher insulin exposure in first 30'
-74% greater insulin action within first 30'



Faster Aspart

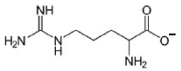


Insulin aspart

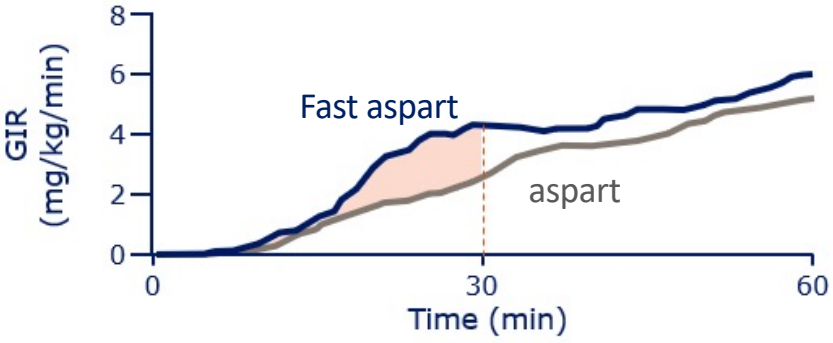
Niacinamide: absorption modifier

Vitamin B3

L-Arginine: added for stability



Naturally occurring amino acid



Selected Summary of Comparative Insulin Trials

1. **Any insulin will lower glucose & A1c; the more injections & the higher the dose, generally the better the control.**

2. **All insulins result in some degree of weight gain & increase the risk of hypoglycemia.**

3. **Adding prandial (food) dosing (i.e., basal-bolus; premixed) will typically reduce A1c greater than basal-only, but at the expense of more weight gain & hypoglycemia.**

4. **Newer basal analogs (degludec [Tresiba®] & glargine U-300 [Toujeo®]) are equally effective in terms of A1c reduction to traditional glargine U-100 (Lantus®, Basaglar® Semglee®), but also associated with slightly less hypoglycemia, mostly overnight.**

"Basal - Bolus" Insulin Therapy

- **"Basal" Insulin (backg**
  - Suppresses HGP betw
  - Nearly constant leve
  - ~ 50% of daily needs
  - Start at 0.2-0.3 U/kg
  - Adjust based on FPG
- **"Bolus" Insulin (mea**
  - Limits post-prandial
  - Immediate rise and s
  - ~ 10-20% of total dai
  - Start at 0.05 U/kg/me
  - Adjust based on 2hr-PG.

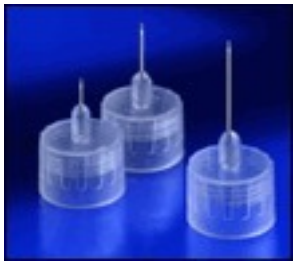
Advanced Bolus Insulin Therapy

1. Dose adjusted by carbohydrate intake ('carb-counting'): e.g., 1 unit ∞ 15 g)
2. Adjust for pre-meal hyperglycemia (similar to a 'sliding scale'): e.g., add 1-2 units for every 50mg/dl starting @150mg/dl.
3. Adjust by anticipated activity level after the meal (e.g., subtract 2-4 units for exercise [or reduce dose by 25-50%].)

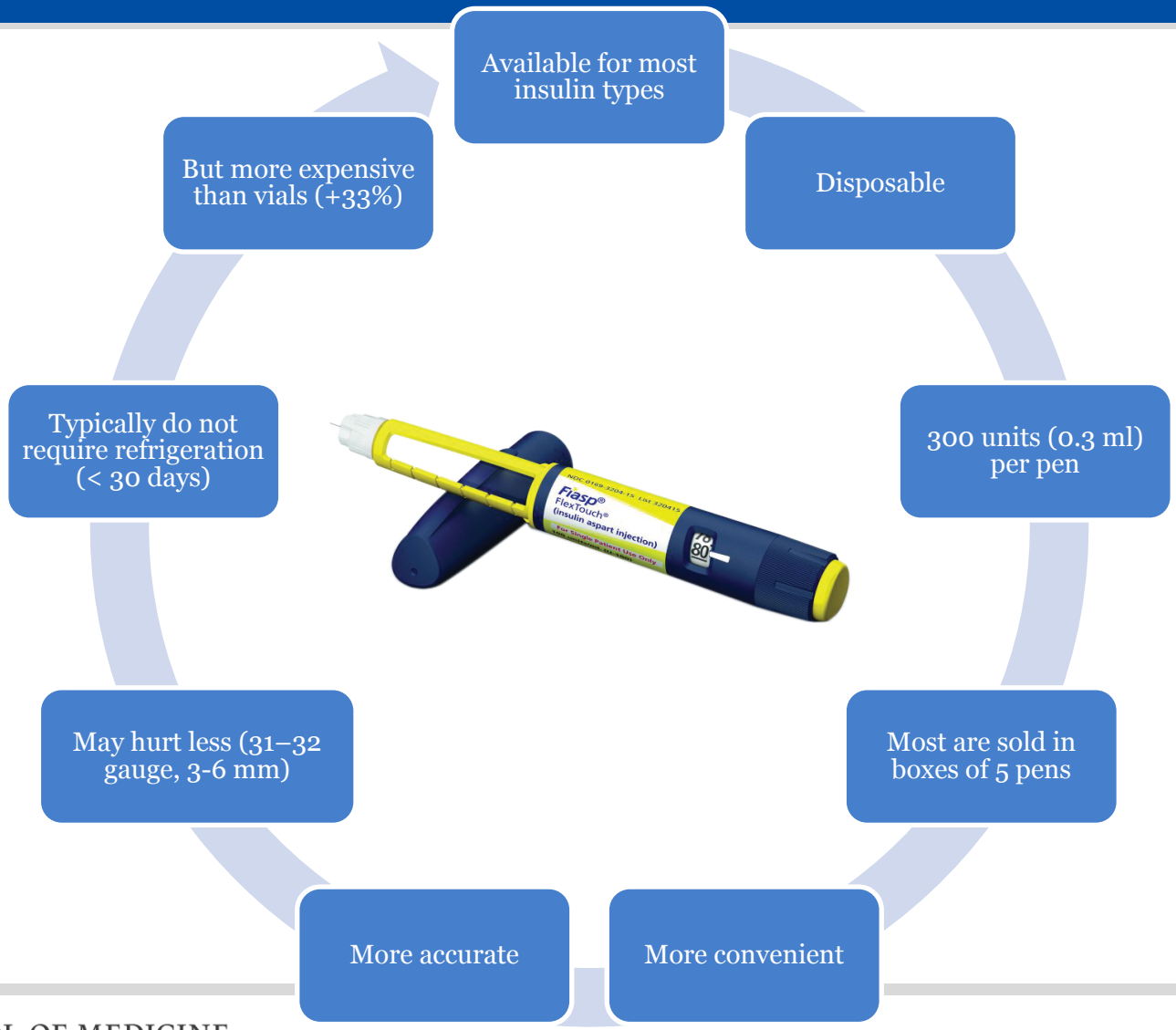
HGP: hepatic glucose production

Edelman SV, Henry RR. Insulin therapy for normalizing glycosylated hemoglobin in type II diabetes: applications, benefits, and risks. *Diabetes Reviews*. 1995;3:308-334;
Kelley DB, ed. *Medical Management of Type 2 Diabetes*. 4th ed. Alexandria, Va: American Diabetes Association; 1998:56-72.

Insulin Pens



Insulin Pens

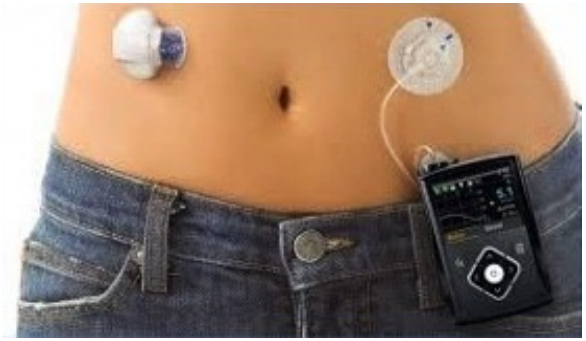


Insulin Costs - H.R.5623 - 117th Congress (2021-2022)

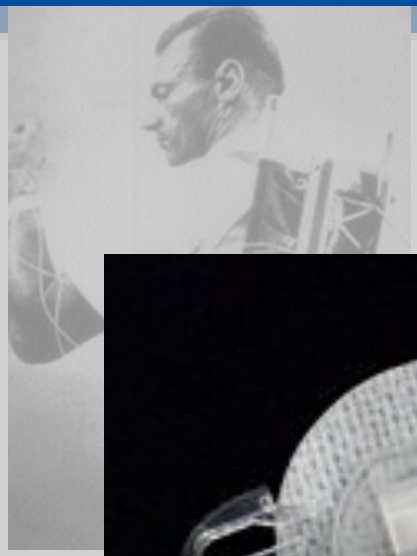
The Affordable Insulin Now Act - H.R.5623

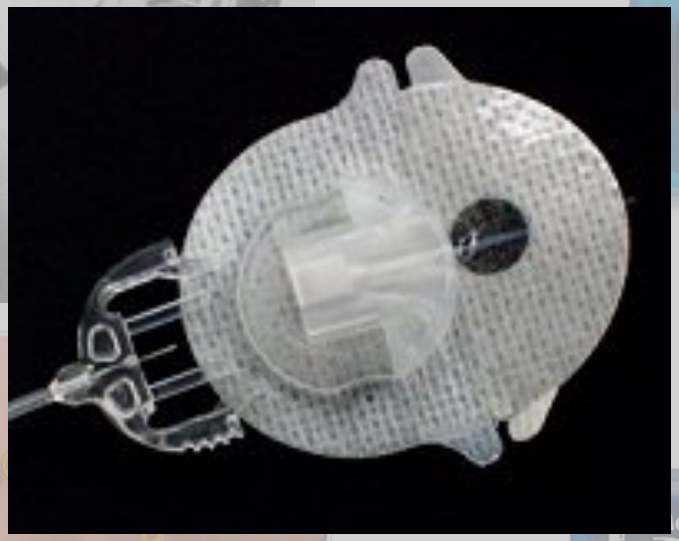
- Bill caps insulin prices at either $35 a month or 25% of an insurance plan's negotiated price — whichever is lower.
- Legislation would take effect in 2023.
- Passed the House with bipartisan support in March 2022.
- Fate in the Senate remains unclear.

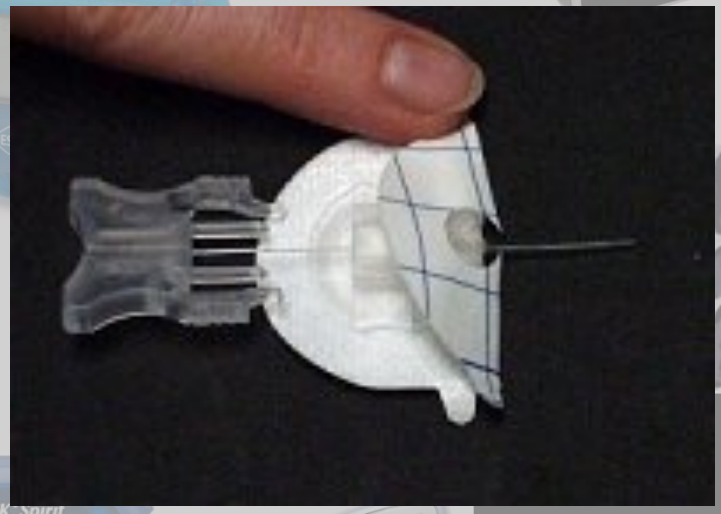
Insulin Pumps

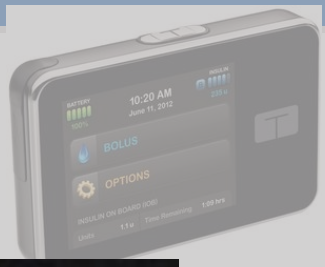


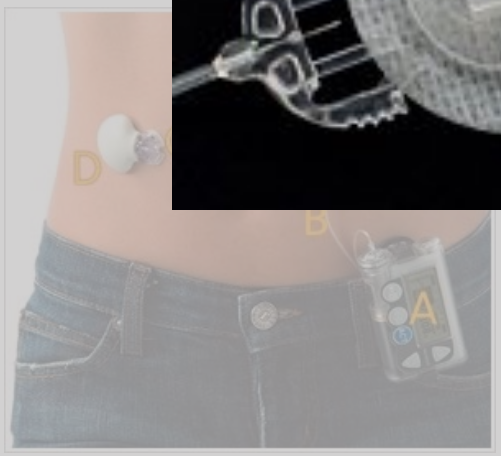
Insulin Pump Infusion Devices











Insulin Pumps: Answers to FAQs

Mainly used in T1DM

SubQ catheter changed q 2-3 days

Variable 24-hour basal rates pre-programmed by clinician

Bolus doses triggered by patient (carb grams entered)

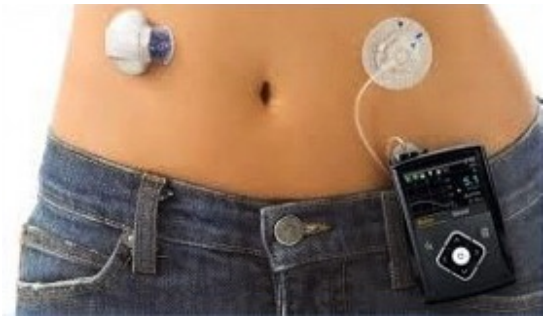
One type of bolus insulin used (rapid analogue)

$6000-7000 pump cost + $10-15/day supply costs

Modestly better control than multiple daily injections (MDI)

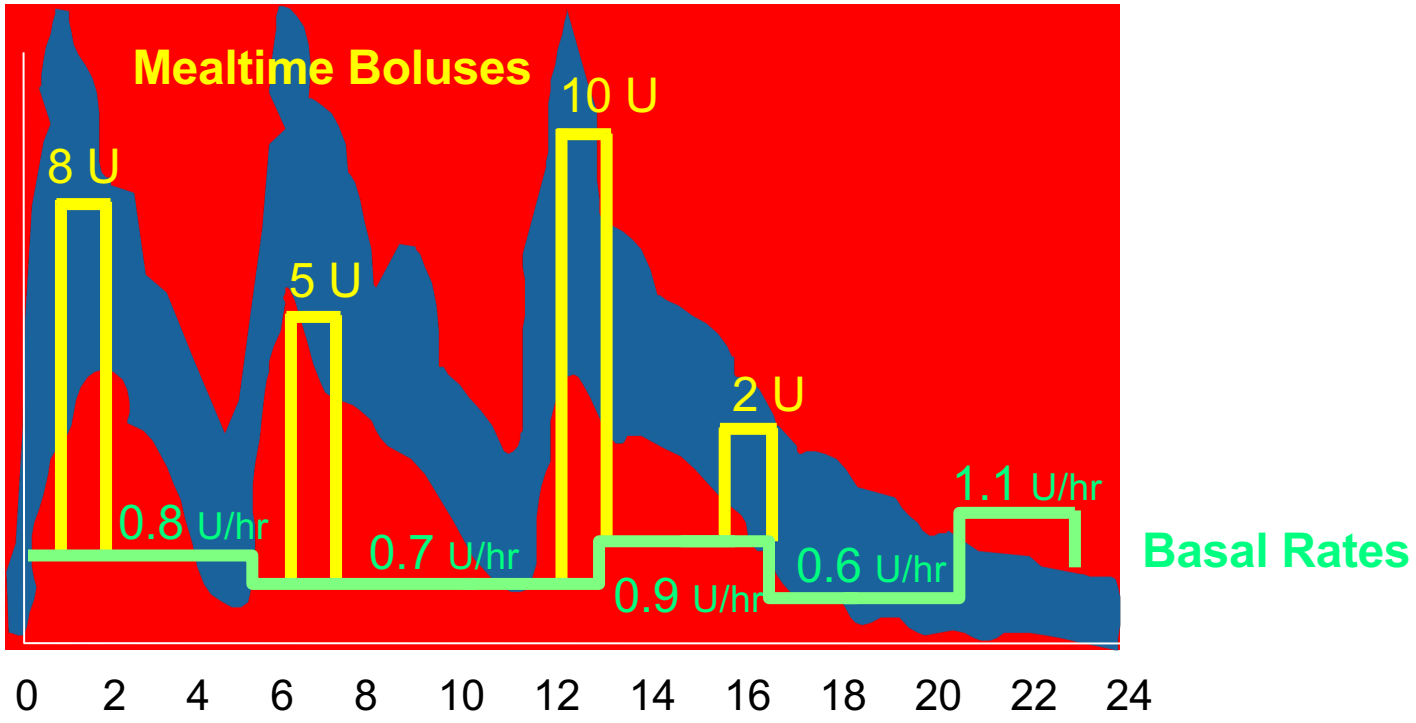
Not typically used in T2DM with MDI but use increasing

Integrated Pump & CGM



- **Reads interstitial glucose continuously, reporting values every 5 minutes**
- **Graphic display for trending information**
- **Sensor changed q 7-14 days**
- **Alarm features**
- **Cloud-based download capabilities, smart-phone enabled**

Continuous Subcutaneous Insulin Infusion (CSII)



Courtesy of Silvio Inzucchi, Yale Endocrinology & Metabolism

Systematic Approach to Patient with Diabetes

Engage & Explore

Screen & Monitor

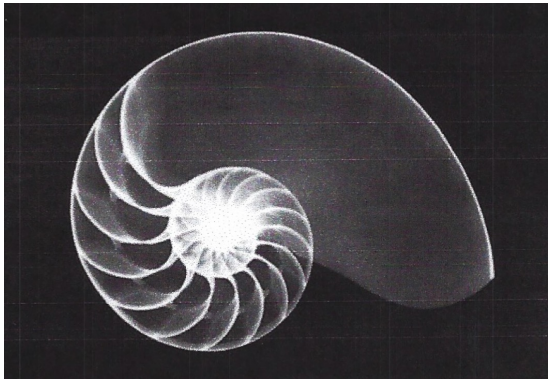
Use Technology

Customize

Support & Follow

Five Practices for Promoting Patient-Centered Care[1,2]

- Prepare with intention
- Listen intently & completely
- Agree on what matters most
- Connect with the patient's story
- Explore emotional cues



JW Chambered Nautilus Approach…

[1]Sanders L, Fortin AH 6th, Schiff GD. Connecting with patients—the missing links. JAMA. 2020;323(1):33-34
[2]Zulman DM, Haverfield MC, Shaw JG, et al. Practices to foster physician presence and connection with patients in the clinical encounter. JAMA. 2020;323(1):70-81.

Patient-Centered Approach to DM Management

Consider patient, disease features, psychology & social network that impact management

Hypoglycemia risk, disease duration, life expectancy, early signs of established vascular complications, etc.

Determine impact of features above on A1C goal & adjust therapeutic strategy accordingly

Revisit & readjust strategy as factors change

ADA. Glycemic Targets. Approach to Individualization of *Diabetes Care.* 2022;45(Suppl.1):S83-S96.

ADA/EASD Management Decision Cycle[1,2]

[1]Decision cycle for patient-centered glycemic management in type 2 diabetes. HbA_{1c}, glycated hemoglobin.
[2]Adapted from Davies MJ, D'Alessio DA, Fradkin J, et al. Diabetes Care 2018;41:2669–2701.
Clin Diabetes. 2022;40(1):10-38. doi:10.2337/cd22-as01

Approach to Patient with BGM or CCM Receiver/Phone

- **Always bring your BG meter or CGM receiver to clinic!**
- **Invite them to show you their BGM or CGM review of data**
  - 7 – 14 – 30 – 90-day averages
  - Percent TBR, TIR, & TAR
  - Pre-meal average histograms
- **BG meter data review usually commences after powering on**
- **Encourage patient to use & become familiar with data review options**
- **Help patient understand how to access BG information**

BGM: Blood glucose monitor; CGM: Continuous glucose monitor

Case 1

- **58 yo with T2DM (2019) & BMI 26 presents ED follow-up.**
- **DM Rx:** Metformin 500mg BID
- **ED:** New symptomatic hyperglycemia - polydipsia & polyuria
  - **HPI:** Patient changed Metformin from BID to daily x 2 mos
  - **A/P:** No DKA; hyperglycemia from med dosing lapse & BID restarted
- **Office f/u:** BGs in 300's & remains symptomatic

Component Latest Ref Rng & Units	11/28/2021	9/13/2021	3/15/2021	9/14/2020	3/6/2020	12/2/2019	5/24/2018	2/1/2018
Hemoglobin A1c <5.7 % of total Hgb	13.8 (H)	6.1	6.2	5.8	7.0	6.0	5.8	7.1 (H)

- **What are you thinking with this patient?**

- **What are the next best steps for patient's management?**

Case 1 – Secondary Causes of Hyperglycemia

- Changes in diet & lifestyle interventions
- Medications
- Destruction of pancreas from chronic pancreatitis, hemochromatosis, pancreatic cancer & cystic fibrosis
- Cushing syndrome, acromegaly & pheochromocytoma
- Gestational diabetes
- Reactive hyperglycemia (postop or in critically ill patients)

Additional History:

- No new meds or substantial changes in diet
- Denied EtOH use
- Wt loss: 4 kg in 3 months
- FHx: Brother with T1DM

Mouri MI, Badireddy M. Hyperglycemia. [Updated 2021 May 10]. In: StatPearls. StatPearls Publishing; 2022 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430900/

Case 1 – Most likely etiologies?

- Non-adherence with meds & diet?
- Increased insulin resistance in setting of glucose toxicity with inadvertent med dosing lapse?
- Progressive insulinopenia? Reclassification as Type 1 DM given FHx of brother with T1DM?
- Occult pancreatic cancer?

Plan:

- **START:** Lantus 12 units daily (0.2u x 60 kg)
- **INCREASE:** Metformin to 1000mg BID
- **CHECK:** GAD 65 Ab, IA-2 Ab, Zinc transporter 8 Ab
- **FOLLOW-UP:** 4 weeks

Mouri MI, Badireddy M. Hyperglycemia. [Updated 2021 May 10]. In: StatPearls. StatPearls Publishing; 2022 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430900/

Case 2

62 yoM with a PMH of T1DM, CAD s/p CABG, s/p Heart transplant, HTN, HLD, Stage 3 CKD

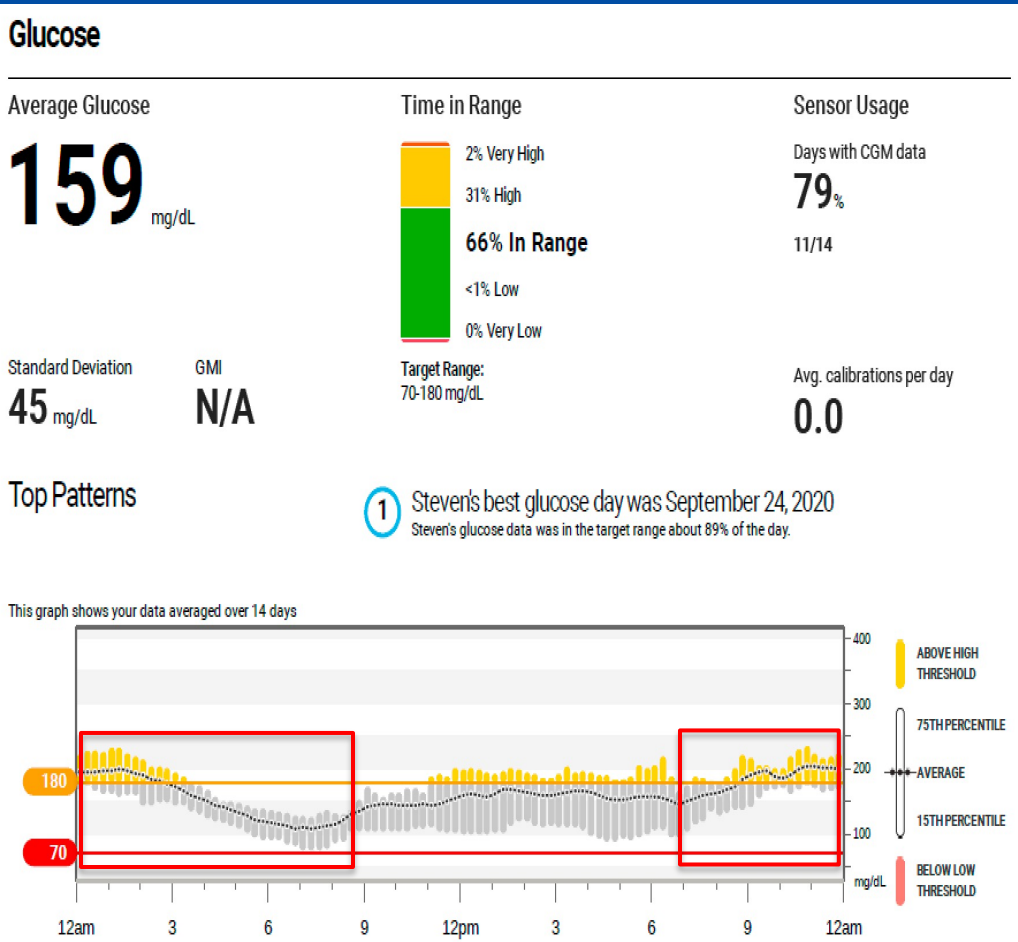
DM Rx:

- Tresiba 35 U at HS (basal insulin)
- Humalog 5u/7u/12u for B/L/D pre-meals

Glucose Monitoring:

- Uses Dexcom G6 CGM

Case 2 – CGM Data period: 9-23-21 to 10-6-2021



Glucose Data Report:

Date of Interpretation:	10/6/2021
Data period:	9/23/21-10/6/2021
Readings:	~4000
Mean BG (mg/dL):	159
Range BG mg/dL):	68-204
% Hyperglycemia (>180):	33%
% at Target (70-180):	66%
% Hypoglycemia (<70):	1%

Average BG (mg/dL) values by meals:

AC Breakfast (FBG):	115
AC Lunch:	160
AC Dinner:	150
HS:	180

1. Trends: steep drop overnight to & mild hypo range by AM
2. PPG spikes to the 200s after supper, sometimes up all night.

Case 2 – Assessment/Plan

Lab Results		
Component	Value	Date
HGBA1C	6.7	10/07/2021
HGBA1C	6.4	06/18/2021
HGBA1C	8.7 (H)	03/16/2021

Assessment:

T2DM - control is quite good.

- BG is trending low in early AM & may be on too much Tresiba.
- BG spikes after supper & are an issue.

Plan:

- **T2DM:**
  1. Decrease Tresiba to 32 U to curb AM lows
  2. Increase supper Humalog to 14 U.

- **CKD-3B:** GFR 41-49; Followed by Nephrology.
- **CVD Risk Reduction:** BP & lipids seem well controlled in past. FLP due for repeat.

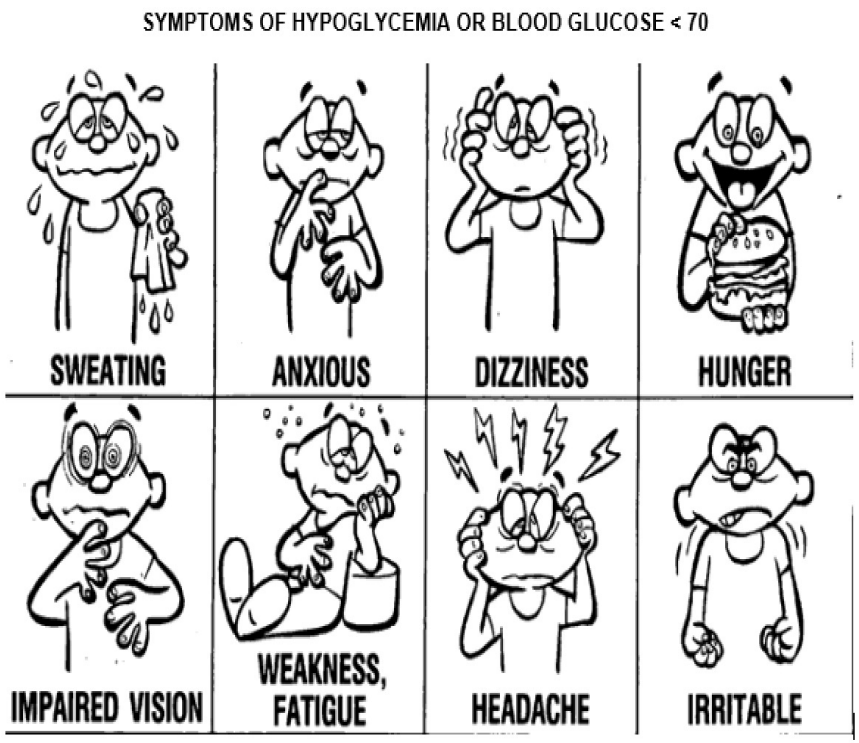
Case 3: Conversion from Pump to Basal/Bolus Insulin

- **32 yo patient with T1DM presents to Urgent Clinic visit.** Insulin pump stopped working. Patient is 90kg.

- Is basal profile or Total Daily Insulin (TDD) retrievable?
  - Total Daily Basal Basal: 46 units

- If basal profile not retrievable, then use kg mass to determine BBC.
  - 92 kg x 0.5 units/24 hours = 46 units total daily insulin requirement
  - **Basal:** 23 units (50%) x 80-85% safety margin – **18-20 units basal**
  - **Bolus:** 23 units (50%):
    - **Breakfast: 5 units**
    - **Lunch: 7 units**
    - **Dinner: 11 units**

Approaches to Hypoglycemia



- **Treat hypos at "alert value" of ≤ 70.**
- **Pure glucose** is preferred treatment, but any glucose-containing carb will raise BG
- **Rule of 15:** 15 gms of carb & recheck in 15 mins
  - Sugary drink 6-8 ounces
  - Banana, orange, grapes or raisins
  - 2-3 Glucose tabs – ~8gms carb/tab
  - Sweet tarts, Skittles or Spree candies (15+)
- **When to use glucagon?**
  - Indicated when unable or unwilling to consume carbohydrates by mouth
  - Newer formulations available: intranasal glucagon & ready-to-inject glucagon
- **Hypoglycemia unawareness**
  - Older adults particularly at risk
  - Relaxation of glucose targets may improve

Now & Future? Islet Cell Transplants

A Cure for Type 1 Diabetes? For One Man, It Seems to Have Worked.

A new treatment using stem cells that produce insulin has surprised experts and given them hope for the 1.5 million Americans living with the disease.

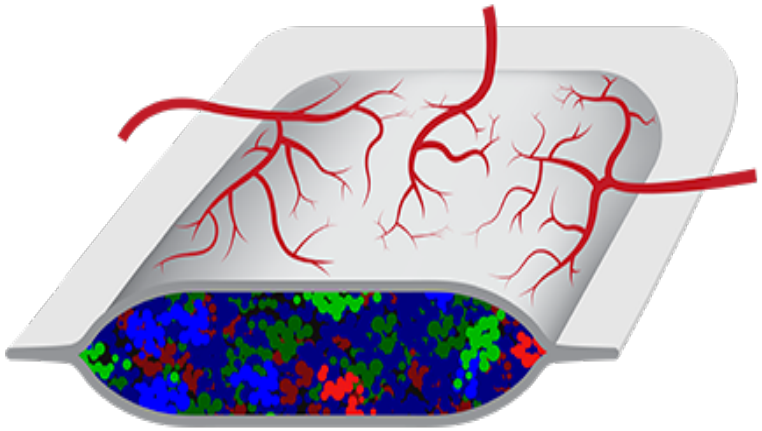
By Gina Kolata

Nov. 27, 2021

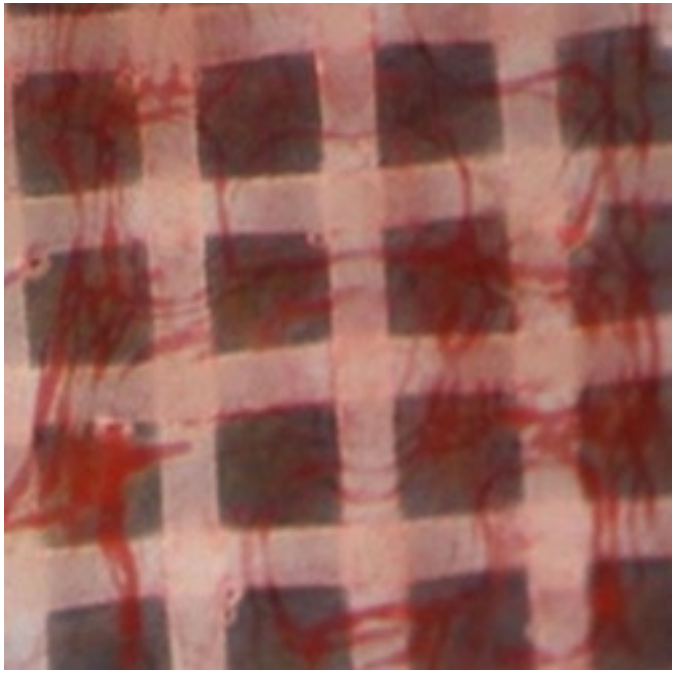
NYT Article: https://www.nytimes.com/2021/11/27/health/diabetes-cure-stem-cells.html

Future? – US FDA & Viacyte: “Artificial Pancreas”

PEC-01 cells in PEC-Direct Product



Vascularization developing at 8 wks



Summary Strategies for Patients with Type 1 Diabetes

1. **If in doubt about diabetes classification, check Islet cell autoantibodies* in adults with suspected T1DM.**
2. **Many insulin types are available & most popular are analogues that better mimic normal insulin dynamics (longer basals & quicker prandials). Cost can be a big issue however!**
3. **Generally, the more complex the regimen, the better the control.**
   - **Optimal strategies: consider patient's capacities for testing, dose calculations, & administration to improve adherence.**
4. **Deciding on best A1c target will strongly inform your decision about which insulin regimen to use.**
5. **CGM is an important tool for glycemic control & for guiding patients on more intensive insulin therapies.**

***Islet cell autoantibodies**: GAD-65, IA2, Zn Transporter 8

Post-Session Questions

1. **What are recommended Time Below Range (TBR) & Time in Range (TIR) blood glucose parameters for patients 18-65 years of age with Type 1 diabetes with no underlying co-morbidities?**

A. > 60% TIR (70-180) & < 4% TBR (<70)
B. > 65% TIR (70-180) & < 4% TBR (<70)
C. > 70% TIR (70-180) & < 4% TBR (<70)
D. > 75% TIR (70-180) & < 4% TBR (<70)

Post-Session Questions

2. When analyzing the Ambulatory Glucose Profile (AGP) for patients with Type 1 or Type 2 diabetes, the top priority for the clinical encounter is to:

A. Minimize hypoglycemia & improve the A1c
B. Minimize hyperglycemia & improve the A1c
C. Minimize hypoglycemia & maintain glucose variability
D. Minimize hypoglycemia & reduce glucose variability

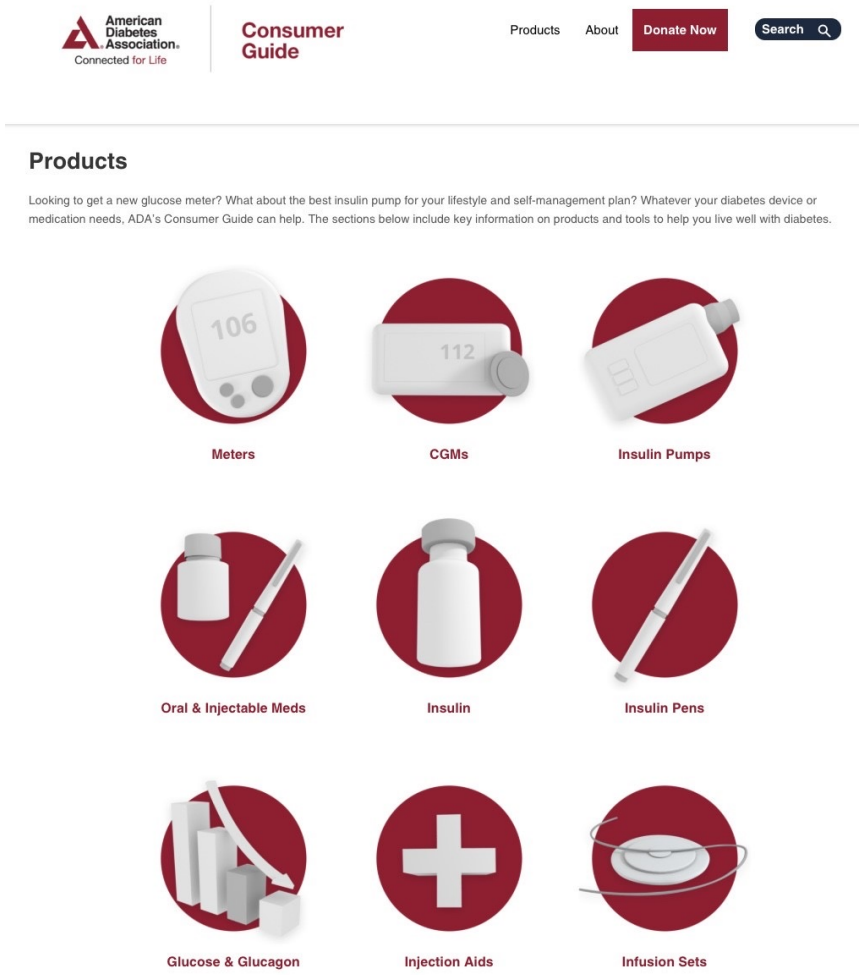
Post-Session Questions

3. The initial diagnostic measure(s) for suspected T1DM proposed by the ADA/EASD in July 2021 include (s):

A. C-peptide
B. GAD antibody
C. C-peptide & GAD antibody
D. GAD antibody & Zinc transporter antibody

ADA Patient/Consumer Guide Link

- ADA Consumer Guide Link
- https://consumerguide.diabetes.org/



References

- *American Diabetes Association. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes—2021. Diabetes Care 2021 Jan; 44(Supplement 1): S111-S124. https://doi.org/10.2337/dc21-S009*
- *American Diabetes Association. Diabetes Technology: Standards of Medical Care in Diabetes—2021. Diabetes Care 2021 Jan; 44(Supplement 1): S85-S99. https://doi.org/10.2337/dc21-S007*
- *De Ferranti SD, Osganian SK. Epidemiology of paediatric metabolic syndrome and type 2 diabetes mellitus. Diab Vasc Dis Res 2007; 4:285. https://pubmed.ncbi.nlm.nih.gov/18158698/*
- *Holt RIG, DeVries JH, Hess-Fischl A, Hirsch IB, Kirkman M. Sue, Klupa T, Ludwig B, Nørgaard K, Pettus J, Renard E, Skyler JS, Snoek FJ, Weinstock RS, Peters AL. The management of type 1 diabetes in adults. A consensus report by the American Diabetes 1 Association (ADA) and the European Association for the Study of Diabetes (EASD). (Draft) ADA's 2021 Scientific Sessions. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8481000/*
- *Mathew TK, Tadi P. Blood Glucose Monitoring. [Updated 2020 Aug 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK555976/*
- *Naylor R, Philipson LH. Who should have genetic testing for maturity-onset diabetes of the young? Clin Endocrinol (Oxf) 2011; 75:422. https://pubmed.ncbi.nlm.nih.gov/21521318/*
- *Pinhas-Hamiel O, Zeitler P. The global spread of type 2 diabetes mellitus in children and adolescents. J Pediatr 2005; 146:693. https://pubmed.ncbi.nlm.nih.gov/15870677/*
- *Ramesh SC, Marshall I. Clinical Suspicion of Maturity Onset of Diabetes of the Young in Pediatric Patients Diagnosed with Diabetes Mellitus. Indian J Pediatr 2012; 79:955. https://pubmed.ncbi.nlm.nih.gov/22161582/*
- *Shah RB, Patel M, Maahs DM, Shah VN. Insulin delivery methods: Past, present and future. Int J Pharm Investig. 2016;6(1):1-9. doi:10.4103/2230-973X.176456*
- *Thanabalasingham G, Owen KR. Diagnosis and management of maturity onset diabetes of the young (MODY). BMJ 2011; 343:d6044. https://pubmed.ncbi.nlm.nih.gov/22012810/*