Type 1 Diabetes

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Disclosures

- None

Learning objectives

- Diagnosis of T1DM (c peptide and beta-cell autoimmune markers)
- Insulin regimen in T1DM
- New technology in T1DM including Insulin pump and CGM use
- Hyperglycemic emergency in T1DM – DKA

Case 1

- **Mr. G, 21 yo male, was diagnosed with T1DM at age 11. On insulin pump for 8 yrs. Weight 99kg. Currently on Medtronic 670G pump with below settings:**
-

Basal rate: (47.5 units per day)
MN 2.05
0430 2.00
0700 1.85
1400 2.00
2000 2.10

ICR
MN 1: 8
0500 1: 4
1000 1: 6
1200 1: 5
1600 1:3.2

ISF
MN 1:28
0530 1:23
1000 1:21
1400 1:22

Blood glucose target:
MN 90-110
0700 80-100
2200 90-110

Date	Result Name	Value	Ind	Ref Range
11/08/2019 9:02	Glucose Level	185 mg/dL	(H)	(65 - 99)
11/08/2019 9:02	Hemoglobin A1c	7.8 %	(H)	(- <=5.6)
11/08/2019 9:02	Estimated Average Glucose (eAG)	177		(Not Established -)
11/08/2019 9:02	BUN	13 mg/dL		(8 - 25)
11/08/2019 9:02	Creatinine	0.92 mg/dL		(0.60 - 1.50)
11/08/2019 9:02	Cholesterol	130 mg/dL		(- <=199)
11/08/2019 9:02	HDL	46 mg/dL		(>=40 -)
11/08/2019 9:02	Cholesterol/HDL Ratio	2.9		(- <=4.9)
11/08/2019 9:02	LDL, Calculation	73 mg/dL		(- <=99)
11/08/2019 9:02	Non HDL Cholesterol	84 mg/dL		(- <=159)
11/08/2019 9:02	Triglycerides	55 mg/dL		(- <=149)
11/08/2019 9:02	VLDL	11 mg/dL		(- <=29)
11/08/2019 9:02	T4 Free	1.3 ng/dL		(0.8 - 1.7)
11/08/2019 9:02	TSH	1.60 mU/L		(0.45 - 4.50)
11/08/2019 9:02	Vitamin D, 25 Hydroxy	16.8 ng/mL	(L)	(>=20.0 -)
11/08/2019 9:02	C Peptide	<0.1 ng/mL	(L)	(1.1 - 4.4)

GAD65ab: negative

Case 2

Ms. N, 39 yo female was diagnosed with T1DM in childhood and on MDI since then.
Weight 100kg.
diabetic regimen:
Levemir 40 units BID, Lispro 20 units TID and Lispro ISF 1:25 over 100 mg/dl

Glucose	**433**	**High**	mg/dL	65 - 99	01
BUN	20		mg/dL	6 - 20	01
Creatinine	0.82		mg/dL	0.57 - 1.00	01
eGFR If NonAfricn Am	90		mL/min/1.73	>59	
eGFR If Africn Am	104		mL/min/1.73	>59	
BUN/Creatinine Ratio	**24**	**High**		9 - 23	
Sodium	139		mmol/L	134 - 144	01
Potassium	4.6		mmol/L	3.5 - 5.2	01
Chloride	101		mmol/L	96 - 106	01
Carbon Dioxide, Total	24		mmol/L	20 - 29	01
Calcium	9.3		mg/dL	8.7 - 10.2	01
Protein, Total	6.4		g/dL	6.0 - 8.5	01
Albumin	3.8		g/dL	3.5 - 5.5	01
Globulin, Total	2.6		g/dL	1.5 - 4.5	
A/G Ratio	1.5			1.2 - 2.2	
Bilirubin, Total	<0.2		mg/dL	0.0 - 1.2	01
Alkaline Phosphatase	70		IU/L	39 - 117	01
AST (SGOT)	9		IU/L	0 - 40	01
ALT (SGPT)	15		IU/L	0 - 32	01
Hemoglobin A1c					
Hemoglobin A1c	**10.4**	**High**	%	4.8 - 5.6	01
Please Note:					01
Prediabetes: 5.7 - 6.4 Diabetes: >6.4 Glycemic control for adults with diabetes: <7.0					
C-Peptide, Serum	2.5		ng/mL	1.1 - 4.4	01

GAD65-ab: negative

GAD65 antibodies and C-peptide

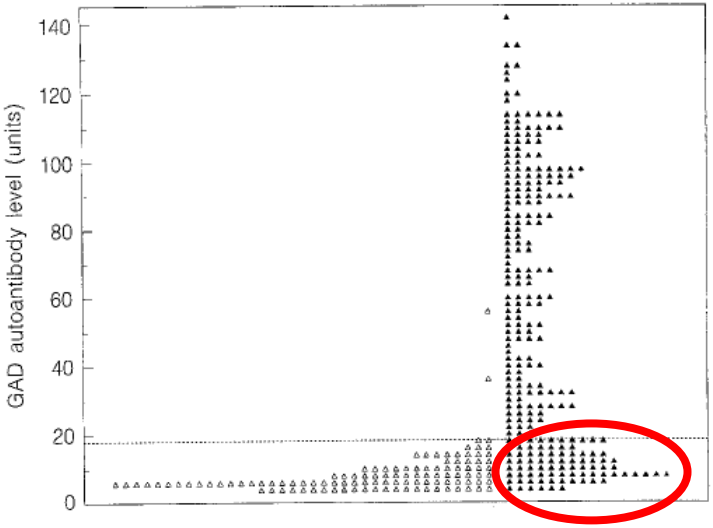

Fig. 1. The levels of antibodies to glutamate decarboxylase (anti-GAD) in 109 non-diabetic children (△) and 261 newly-diagnosed diabetic children (▲). The dashed line represents the 98th percentile for anti-GAD among the non-diabetic children (18 units)

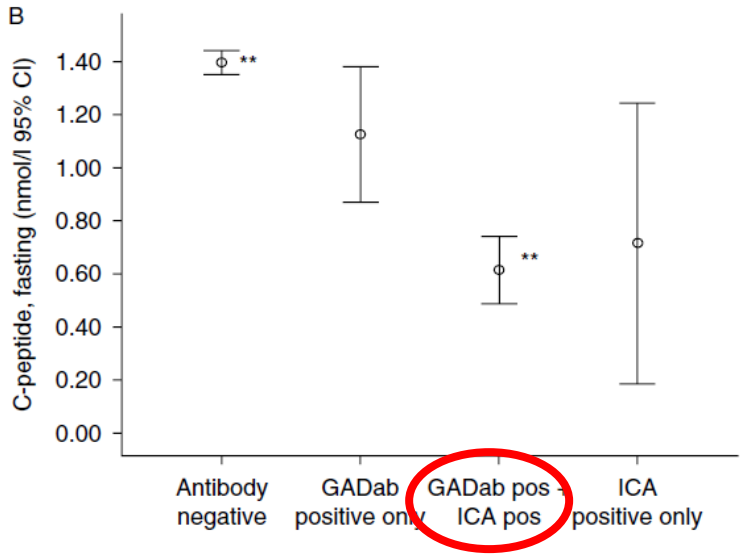

Figure 1 (A) Mean fasting C-peptide (nmol/l), per age and BMI group in non-autoimmune diabetes. (B) Mean fasting C-peptide, including 95% confidence intervals, per antibody positivity; all in adults with newly diagnosed diabetes. $^{**}P<0.001$.

Verge CF, et al. Anti-glutamate decarboxylase and other antibodies at the onset of childhood IDDM: a population-based study. *Diabetologia* 1994 37 1113–1120.

Thunander M, et al. Levels of C-peptide, body mass index and age, and their usefulness in classification of diabetes in relation to autoimmunity, in adults with newly diagnosed diabetes in Kronoberg, Sweden. Eur J Endocrinol. 2012 Jun;166(6):1021-9.

Case 3

A 79 yo male with a history of metastatic malignant melanoma, who received Pembrolizumab, presented to the ED with polyuria, polydipsia and weakness. He was noted to have serum glucose 1150 mg/dl, CO2 13, AG 26, and Beta-hydroxybutyrate 124, Ph7.16. GAD65ab negative, C peptide 1.1 ng/ml (1.1-4.4) at presentation in 11/2017. C peptide <0.1 ng/ml in 2/2020. What type of diabetes does he have?

A. LADA (Latent autoimmune diabetes in adults)

B. T2DM

C. Ketosis prone diabetes

D. Pembrolizumab-induced T1DM

T1DM and Immune checkpoint inhibitor

Table 4 Summary of results.

Characteristic	All cases (*n* = 91)
Age, years	
Median (range)	61 (22–84)
Gender	
Female/male	36 vs 55
Ethnicity	
Asian	14/91 (15%)
Tumor types	
Melanoma	48/91 (53%)
NSCLC	14/91 (15%)
Past medical history*	20/91 (22%)
Prior immunotherapy	22/91 (24%)
IL-2	2/91
Interferon	7/91
Ipilimumab	16/91
Nivolumab	3/91
Immune checkpoint inhibitor	
Anti-CTLA-4	3/91 (3%)
Anti-PD-1	65/91 (71%)
Anti-PD-L1	7/91 (8%)
Anti-CTLA-4 + anti-PD-1	14/91 (15%)
Anti-PD-L1 + 4-1BB blockade	1/91
CTLA-4 or PD-1 blockade	1/91
Time-to-diagnosis in cycles (range)	4.5 (1–17)
Combination therapy	2.7 (1–5)
With/without DKA	4 vs 5.9
GADA pos./GADA neg.	3.1 vs 5.9
Diabetic ketoacidosis	64/91 (71%)
Glycemia, median (range)	565 mg/dL (209–1211)
Glycated hemoglobin, median (range)	7.6% (5.4–11.4)
Low-C-peptide at diagnosis	58/69 (84%)
Elevated lipase	13/25 (52%)
Positive pancreas autoantibodies	
At least one	47/88 (53%)
Two or more	13/88 (15%)
Type of pancreas autoantibodies	
GADA	51%
IA-2	18%
ICA	13%
Anti-insulin	26%
ZnT8	4%
HLA analysis	51/91 (56%)
Susceptible	31/51 (61%)
Susceptible and protective	2/51 (4%)
Neutral	10/51 (20%)
Protective	8/51 (16%)
Thyroid dysfunction with ICI	21/91 (24%)
Prior history of thyroid dysfunction	2/21

*Diabetes mellitus, thyroid disease or risk thereof.
4-1BB, CD137; CTLA-4, cytotoxic T lymphocyte antigen 4; DKA, diabetes ketoacidosis; GADA, glutamic acid decarboxylase; HLA, human leukocyte antigen; IA-2, insulinoma-associated antigen-2; ICA, islet-cell antibodies; ICI, immune checkpoint inhibitor; IL-2, Interleukin-2; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; ZnT8, zinc transporter 8.

de Filette JMK, et al. Immune checkpoint inhibitors and type 1 diabetes mellitus: a case report and systematic review. Eur J Endocrinol. 2019 Jul.

Classification of Diabetes

CLASSIFICATION

Diabetes can be classified into the following general categories:

1. Type 1 diabetes (due to autoimmune β-cell destruction, usually leading to absolute insulin deficiency, including latent autoimmune diabetes of adulthood)
2. Type 2 diabetes (due to a progressive loss of adequate β-cell insulin secretion frequently on the background of insulin resistance)
3. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation)
4. Gestational diabetes mellitus (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation)

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Staging 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.

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Criteria for the diagnosis of Diabetes

Table 2.2—Criteria for the diagnosis of diabetes

FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*
OR
2-h PG ≥200 mg/dL (11.1 mmol/L) during OGTT. The test should be performed as described by WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*
OR
A1C ≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*
OR
In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

DCCT, Diabetes Control and Complications Trial; FPG, fasting plasma glucose; OGTT, oral glucose tolerance test; WHO, World Health Organization; 2-h PG, 2-h plasma glucose. *In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results from the same sample or in two separate test samples.

- **Plasma glucose not a1c should be used to diagnose the acute onset of T1DM.**
- **Autoimmune markers: islet cell autoantibodies, GAD65-ab, insulin, the tyrosine phosphatases IA-2 and IA-2B and zinc transporter 8 (ZnT8).**

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Case 4

A 23 yo female with T1DM called you because her glucose level was 400 mg/dl. She wanted to know what she should do with glucose level at 400 mg/dl.

Her home diabetic regimen: Lantus 15 units Qhs, Humalog 5 units TID. Her body weight is 60 kg. She has no correction scale. Her glucose goal is 100 mg/dl.

A. Give 6 units of Humalog

B. Give 3 units of Humalog

C. Give 15 units of Humalog

D. Give 10 units of Humalog

$$\frac{400 - 100}{\text{Correction factor}}$$

Useful Insulin Formulas

- **The carbohydrate coverage ratio: 500 ÷ Total Daily Insulin Dose**
  = 1 unit insulin covers X many grams of carbohydrate

  Eg, total insulin dose 50 units per day gives you carb ratio 1 u: 10 gram

- **Insulin sensitivity (IS) or correction factor** (CF)

  Correction Factor = 1800 ÷Total Daily Insulin Dose = 1 unit of insulin will reduce the blood sugar how many mg/dl.

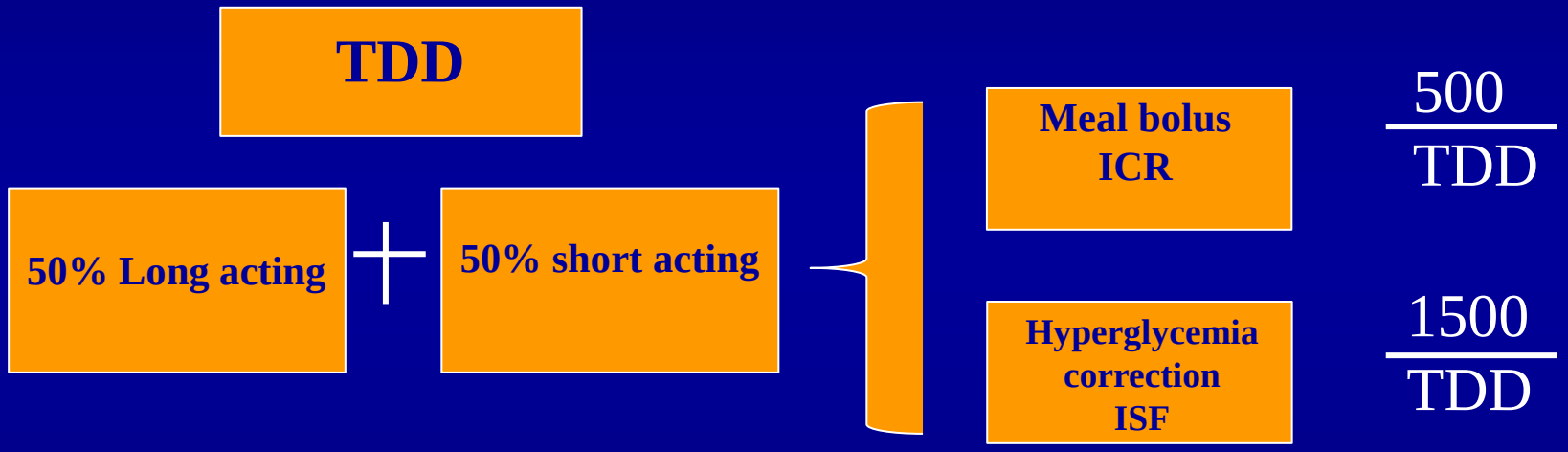
  (some use1500 reg/1800 rapid-acting insulin)

- If you measure your body weight in kilograms:

  Total Daily Insulin Requirement (in units of insulin)
  = 0.50 X Total Weight in Kilograms (E.g, 100 kg= 55 units)

Initial TDD (total daily insulin dose)

- **TDD = wt (kg) x 0.5 – T1DM, Wt (Kg) x 0.3 - pt with CKD**
- **TDD = wt (kg) x 0.7-1.0 – for obese / insulin resistant pt**



TDD = 30 units/day. ICR 1:16. ISF 1:50 over BG target
TDD = 50 units/day. ICR 1:10. ISF 1:30 over BG target
TDD = 100 units/day. ICR 1:5. ISF 1:15 over BG target

Pharmacologic Therapy for T1DM

- **Most people with type 1 diabetes should be treated with multiple daily injections (MDI) of prandial and basal insulin, or continuous subcutaneous insulin infusion (insulin pump).**

- **Most individuals with type 1 diabetes should use rapid-acting insulin analogs to reduce hypoglycemia risk.**

- **Patients with type 1 diabetes should be trained to match prandial insulin doses to carbohydrate intake, premeal blood glucose, and anticipated physical activity.**

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Insulin Development

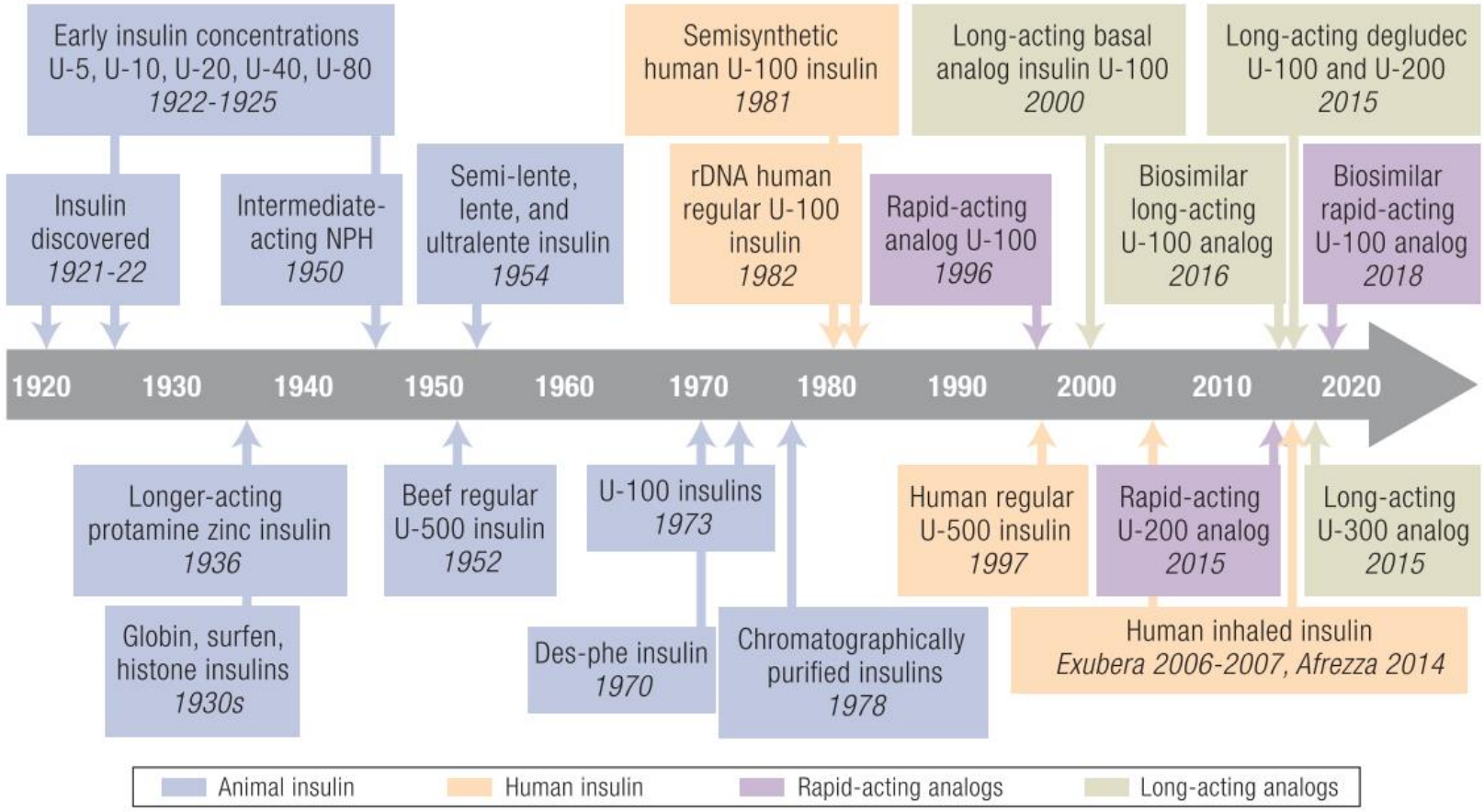


Figure 1. Timeline of insulin development with approximate historical dates. Abbreviations: NPH, neutral protamine Hagedorn; rDNA, recombinant DNA; U = units.

Hirsch I, The Evolution of Insulin and How it Informs Therapy and Treatment Choices. Endocrine Review 2020, Oct 1.

Time-action of insulin

Table 1. Time-action of rapid-acting insulin analogs versus human regular insulin.

Insulin Type	Brand name	Onset of Action (min)	Peak Action (hr)	Duration of Action (hr)
Short-acting				
Human regular insulin	Humulin® R Novolin® R Insuman® R	30–60	2–4	5–8
Rapid-acting				
Insulin lispro	Humalog®, Admelog	15–30	0.5–2.5	≤5
Insulin aspart	Novolog® (26)	15	1–3	3–5
Insulin glulisine	Apidra®	12–30	1.5	~5.3
Faster rapid-acting				
Faster insulin aspart	Fiasp® (30)	~16–20	~1.5–2.2	~5–7
Inhaled human insulin	Afrezza® (34)	~12	0.5–0.9	1.5–3

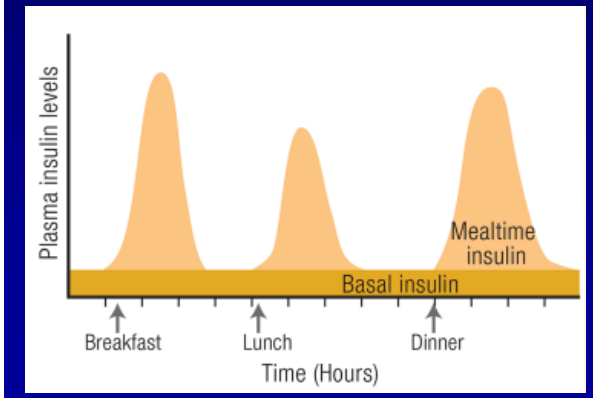
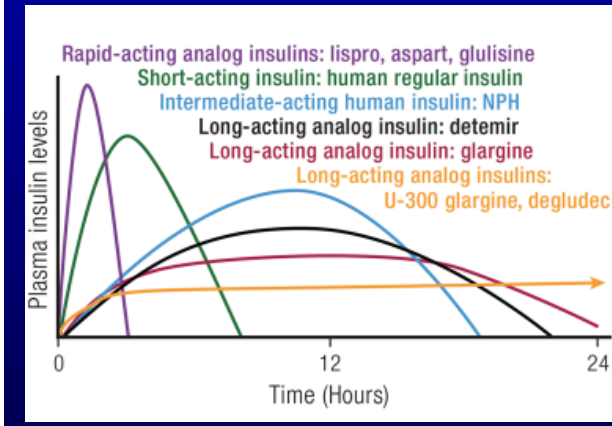


Table 2. Time-action of intermediate-acting and long-acting insulins (100 U/mL).

Insulin Type	Brand name	Onset of Action (hr)[a]	Peak Action (hr)	Duration of Action (hr)
Intermediate-acting U-100				
NPH insulin	Humulin® N (40), Novolin® N (41)	1–2	2–8	14–24
Long-acting U-100				
Insulin glargine	Lantus® (43), Basaglar®	NA	No pronounced peak	24
Insulin detemir	Levemir® (52)	NA	No pronounced peak	7.6–>24
Insulin degludec	Tresiba® (59)	NA	No pronounced peak	42



Hirsch I, The Evolution of Insulin and How it Informs Therapy and Treatment Choices. Endocrine Review 2020, Oct 1.

Premixed insulin

Table 3. Premixed insulins currently available in the United States.

Brand Name	Components	Peak Action (min)
Human insulin mixtures		
Humulin® 70/30 Novolin® 70/30	70% human NPH insulin; 30% human regular insulin	132 (68)
Analog insulin mixtures		
Humalog® mix 75/25	75% insulin lispro protamine suspension; 25% insulin lispro	94 (69)
Humalog® mix 50/50	50% insulin lispro protamine suspension; 50% insulin lispro	81 (70)
NovoLog® mix 70/30	70% insulin aspart protamine suspension; 30% insulin aspart	162 (71)
Ryzodeg® 70/30	70% insulin degludec; 30% insulin aspart	72 (73)

Hirsch I, The Evolution of Insulin and How it Informs Therapy and Treatment Choices. Endocrine Review 2020, Oct 1.

Concentrated insulin

Table 4. Concentrated insulins currently available in the United States.

Insulin Name	Concentration	Brand Name	Insulin Type	Notes
Bioequivalent to reference 100 U/mL				• Equivalent time-action profiles. • No dose adjustment needed.
Insulin lispro	200 U/mL	Humalog®	Prandial analog	
Insulin degludec	200 U/mL	Tresiba®	Basal analog	
Nonbioequivalent to reference 100 U/mL				• Different time-action profiles. • Dose adjustment needed for U-300. • No dose adjustment required for U-500R.
Insulin glargine	300 U/mL	Toujeo®	Basal analog	
Human regular insulin	500 U/mL	Humulin® R U-500	Prandial/basal human	

Hirsch I, The Evolution of Insulin and How it Informs Therapy and Treatment Choices. Endocrine Review 2020, Oct 1.

Concentrated Insulin

Table 1 – Concentrated insulins currently available.

	Regular U-500[a,b]	Regular U-500[a,b]	Glargine U-300[a,c]	Glargine U-300[c]	Degludec U-200[a,d,e]	Lispro U-200[a,e,f]
Device	Vial	Pen	Pen	Pen	Pen	Pen
PK/PD characteristics	Prandial and basal	Prandial and basal	Basal	Basal	Basal	Prandial
Bioequivalent	No	No	No	No	Yes	Yes
Unit increments	5	5	1	2	2	1
Maximum dose (Units)	250 [g]	300	80	160	160	60
Units/device	10,000	1500	450	900	600	600
Storage and handling in use (days)	40	28	42	42	56	28
Minimum daily units[h]	250[i]	54[i]	11	20	11	21

Regular U-500, regular U-500 insulin (Humulin®); Glargine U-300, insulin glargine U-300 (Toujeo®); Degludec U-200, insulin degludec U-200 (Tresiba®); Lispro U-200, insulin lispro U-200 (Humalog 200®); PD, pharmacodynamics; PK, pharmacokinetics.

[a] Hood. *Diabetes Technol Ther* 2017; 19(4): 203–5.

[b] HUMULIN® Prescribing Information, 2016.

[c] TOUJEO® Prescribing Information, 2018.

[d] TRESIBA® Prescribing Information, 2018.

[e] Ovalle et al. *Curr Med Res Op* 2018; 34(6): 1029–1043.

[f] HUMALOG®, Prescribing Information, 2017.

[g] Using dedicated U-500 syringe.

[h] Minimum needed to empty the device before contents expire.

[i] Indicated for people with diabetes requiring > 200 units of daily insulin.

Schloot NC, et al. Concentrated insulins in current clinical practice. Diabetes Res Clin Pract. 2019 Feb;148:93-101.

Median cost of insulin products

Table 9.4—Median cost of insulin products in the U.S. calculated as AWP (70) and NADAC (71) per 1,000 units of specified dosage form/product

Insulins	Compounds	Dosage form/product	Median AWP (min, max)*	Median NADAC*
Rapid-acting	• Lispro follow-on product	U-100 vial	$157	$125
		U-100 prefilled pen	$202	$161
	• Lispro	U-100 vial	$165†	$132†
		U-100 cartridge	$408	$325
		U-100 prefilled pen	$212†	$170†
		U-200 prefilled pen	$424	$339
	• Lispro-aabc	U-100 vial	$330	N/A
		U-100 prefilled pen	$424	N/A
		U-200 prefilled pen	$424	N/A
	• Glulisine	U-100 vial	$341	$272
		U-100 prefilled pen	$439	$352
	• Aspart	U-100 vial	$174†	$139†
		U-100 cartridge	$215	$172
		U-100 prefilled pen	$223†	$179†
	• Aspart ("faster acting product")	U-100 vial	$347	$278
		U-100 cartridge	$430	N/A
		U-100 prefilled pen	$447	$356
	• Inhaled insulin	Inhalation cartridges	$1,325	$606
Short-acting	• human regular	U-100 vial	$165††	$132††
		U-100 prefilled pen	$208	$167
Intermediate-acting	• human NPH	U-100 vial	$165††	$132††
		U-100 prefilled pen	$208	$167
Concentrated human regular insulin	• U-500 human regular insulin	U-500 vial	$178	$143
		U-500 prefilled pen	$230	$184
Long-acting	• Glargine follow-on products	U-100 prefilled pen	$118	$96
		U-100 vial	$190 (118, 261)	$95
	• Glargine	U-100 vial; U-100 prefilled pen	$340	$277
		U-300 prefilled pen	$340	$272
	• Detemir	U-100 vial; U-100 prefilled pen	$370	$296
	• Degludec	U-100 vial; U-100 prefilled pen; U-200 prefilled pen	$407	$325
Premixed insulin products	• NPH/regular 70/30	U-100 vial	$165††	$133††
		U-100 prefilled pen	$208	$167
	• Lispro 50/50	U-100 vial	$342	$274
		U-100 prefilled pen	$424	$338
	• Lispro 75/25	U-100 vial	$152	$273
		U-100 prefilled pen	$212	$170
	• Aspart 70/30	U-100 vial	$180	$144
		U-100 prefilled pen	$224	$179
Premixed insulin/GLP-1 RA products	• Glargine/Lixisenatide	100/33 μg prefilled pen	$619	$495
	• Degludec/Liraglutide	100/3.6 μg prefilled pen	$917	$732

AWP, average wholesale price; GLP-1 RA, glucagon-like peptide 1 receptor agonist; N/A, not available; NADAC, National Average Drug Acquisition Cost. *AWP or NADAC calculated as in **Table 9.3**. †Generic prices used when available. ††AWP and NADAC data presented do not include vials of regular human insulin and NPH available at Walmart for approximately $25/vial; median listed alone when only one product and/or price.

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- 100 test strips $17.88

Prime Test Strips
- 25 test strips $5.00
- 50 test strips $9.00
- 100 test strips $17.88

Human Insulin

Novolin®/ReliOn™ (recombinant DNA origin) is manufactured for Walmart by Novo Nordisk

Novolin®/ReliOn™ Insulin Pens
$42.88

Novolin®/ReliOn™ Insulin* ... $24.88
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*This product is available behind the pharmacy counter, ask your Walmart pharmacist. Pricing is subject to change. Pricing not available in Alaska, Hawaii, Puerto Rico.

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Ketone Strips

Ketone Test Strips
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Insulin delivery approaches in T1DM

Representative relative attributes of insulin delivery approaches in people with type 1 diabetes[1]

Injected insulin regimens	Flexibility	Lower risk of hypoglycemia	Higher costs
MDI with LAA + RAA or URAA	+++	+++	+++
Less-preferred, alternative injected insulin regimens			
MDI with NPH + RAA or URAA	++	++	++
MDI with NPH + short-acting (regular) insulin	++	+	+
Two daily injections with NPH + short-acting (regular) insulin or premixed	+	+	+

Continuous insulin infusion regimens	Flexibility	Lower risk of hypoglycemia	Higher costs
Hybrid closed-loop technology	+++++	+++++	++++++
Insulin pump with threshold/ predictive low-glucose suspend	++++	++++	+++++
Insulin pump therapy without automation	+++	+++	++++

Figure 9.1—Choices of insulin regimens in people with type 1 diabetes. Continuous glucose monitoring improves outcomes with injected or infused insulin and is superior to blood glucose monitoring. Inhaled insulin may be used in place of injectable prandial insulin in the U.S. [1]The number of plus signs (+) is an estimate of relative association of the regimen with increased flexibility, lower risk of hypoglycemia, and higher costs between the considered regimens. LAA, long-acting insulin analog; MDI, multiple daily injections; RAA, rapid-acting insulin analog; URAA, ultra-rapid-acting insulin analog. Reprinted from Holt et al. (5).

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Case 5

A 21 yo male with T1DM has been on multiple daily injections (MDI) since age 11. His recent a1c was 9%. He is comfortable on carb counting. He eats meals frequently and only boluses before his bigger meals. He has lows before midnight but has hyperglycemia in the morning. He wanted to know other choices to improve his diabetes control. Which one is the best next step?

A. Continue MDI

B. Continue MDI and start continuous glucose monitoring (CGM)

C. Insulin pump with CGM

D. Closed-loop insulin pump system

Continuous glucose monitoring (CGM)

Table 7.3—Continuous glucose monitoring devices

Type of CGM	Description
rtCGM	CGM systems that measure and store glucose levels continuously and without prompting
isCGM with and without alarms	CGM systems that measure glucose levels continuously but require scanning for storage of glucose values
Professional CGM	CGM devices that are placed on the patient in the provider's office (or with remote instruction) and worn for a discrete period of time (generally 7–14 days). Data may be blinded or visible to the person wearing the device. The data are used to assess glycemic patterns and trends. These devices are not fully owned by the patient—they are clinic-based devices, as opposed to the patient-owned rtCGM/isCGM devices.

CGM, continuous glucose monitoring; isCGM, intermittently scanned CGM; rtCGM, real-time CGM.

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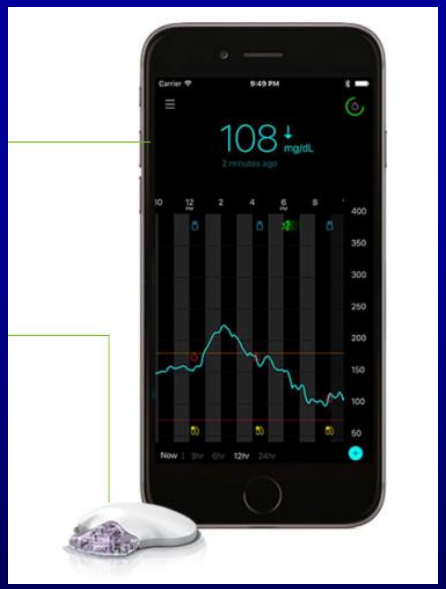
Continuous glucose monitoring (CGM)

FreeStyle Libre 2

Dexcom CGM G6

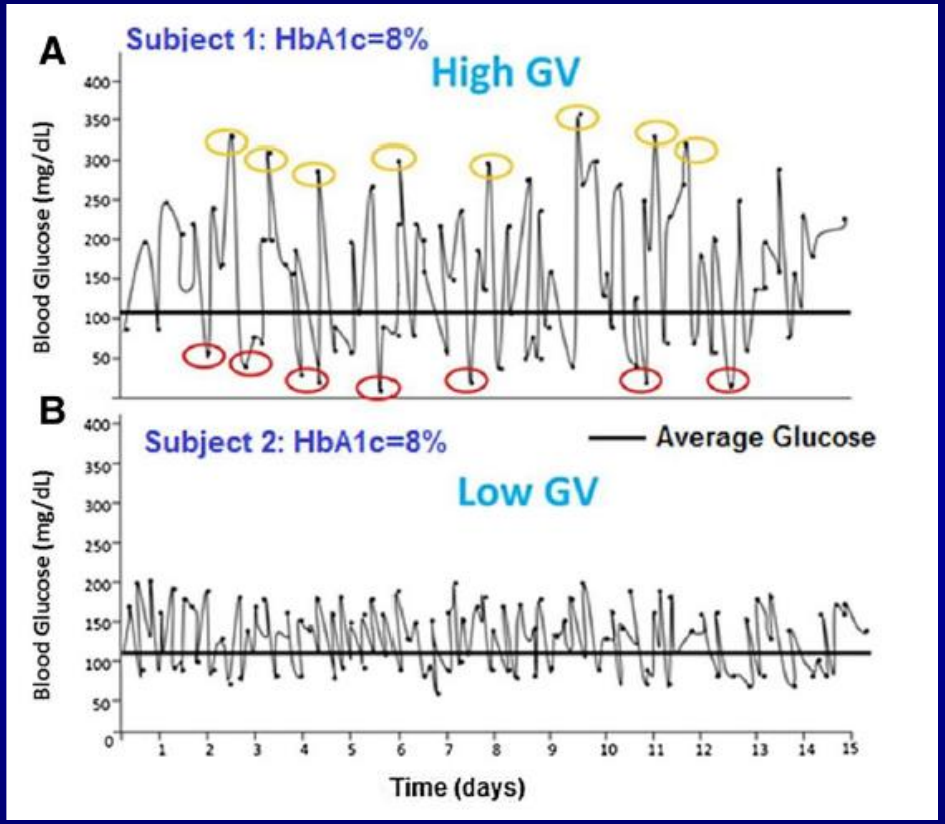


Medtronic Guandian Connect CGM

Continuous Glucose Monitoring (CGM)

Table 1 New definitions of hypoglycemia, hyperglycemia, and time in glycemic range

Outcome	Definition
Hypoglycemia	Level 1: glucose < 70 mg/dL (3.9 mmol/L) and glucose ≥ 54 mg/dl (3.0 mmol/L)
	Level 2: glucose < 54 mg/dL (3.0 mmol/L)
	Level 3: a severe event characterized by altered mental and/or physical status requiring assistance
Hyperglycemia	Level 1 (elevated glucose): glucose > 180 mg/dL (10 mmol/L) and glucose ≤ 250 mg/dlL(13.9 mmol/L)
	Level 2 (very elevated glucose): glucose > 250 mg/dL (13.9 mmol/L)
Time in range	Percentage of readings in the range of 70–180 mg/dL (3.9–10.0 mmol/L) per unit of time



Chehregosha H, et al. A View Beyond HbA1c: Role of Continuous Glucose Monitoring . Diabetes Ther, 2019 Jun;10(3):853-863.

CGM metrics and AGP

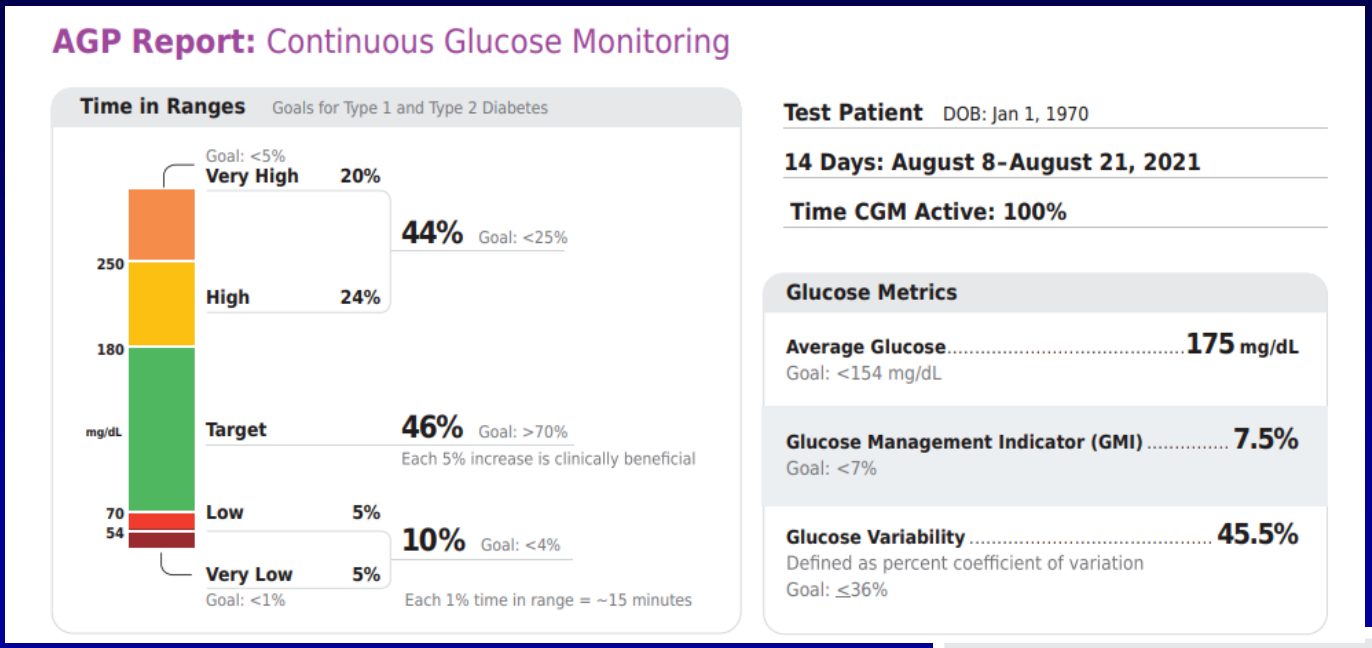


Table 6.2—Standardized CGM metrics for clinical care

1. Number of days CGM device is worn (recommend 14 days)	
2. Percentage of time CGM device is active (recommend 70% of data from 14 days)	
3. Mean glucose	
4. Glucose management indicator	
5. Glycemic variability (%CV) target ≤36%*	
6. TAR: % of readings and time >250 mg/dL (>13.9 mmol/L)	Level 2 hyperglycemia
7. TAR: % of readings and time 181–250 mg/dL (10.1–13.9 mmol/L)	Level 1 hyperglycemia
8. TIR: % of readings and time 70–180 mg/dL (3.9–10.0 mmol/L)	In range
9. TBR: % of readings and time 54–69 mg/dL (3.0–3.8 mmol/L)	Level 1 hypoglycemia
10. TBR: % of readings and time <54 mg/dL (<3.0 mmol/L)	Level 2 hypoglycemia

CGM, continuous glucose monitoring; CV, coefficient of variation; TAR, time above range; TBR, time below range; TIR, time in range. *Some studies suggest that lower %CV targets (<33%) provide additional protection against hypoglycemia for those receiving insulin or sulfonylureas. Adapted from Battelino et al. (34).

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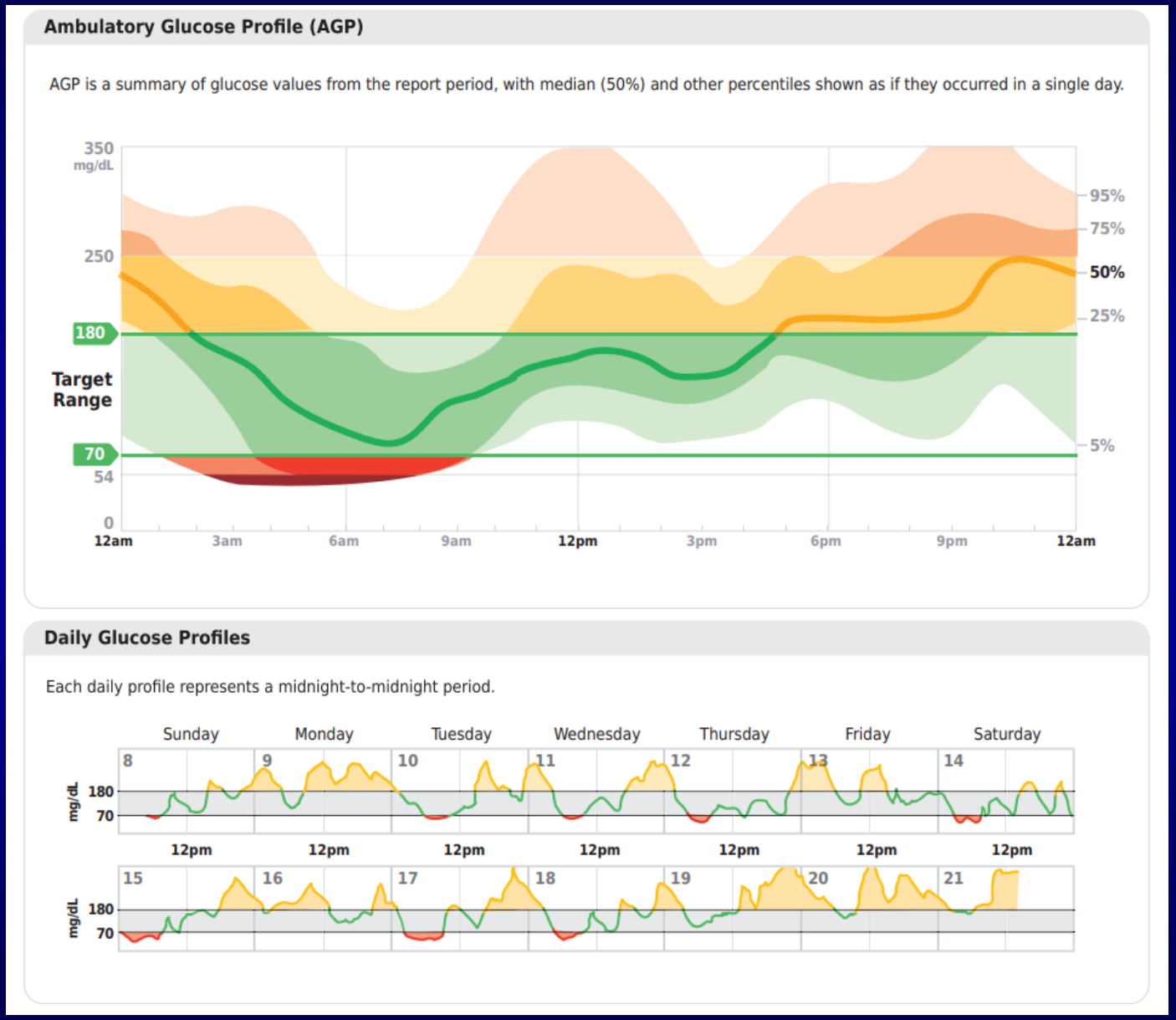
Ambulatory Glucose Profile - AGP



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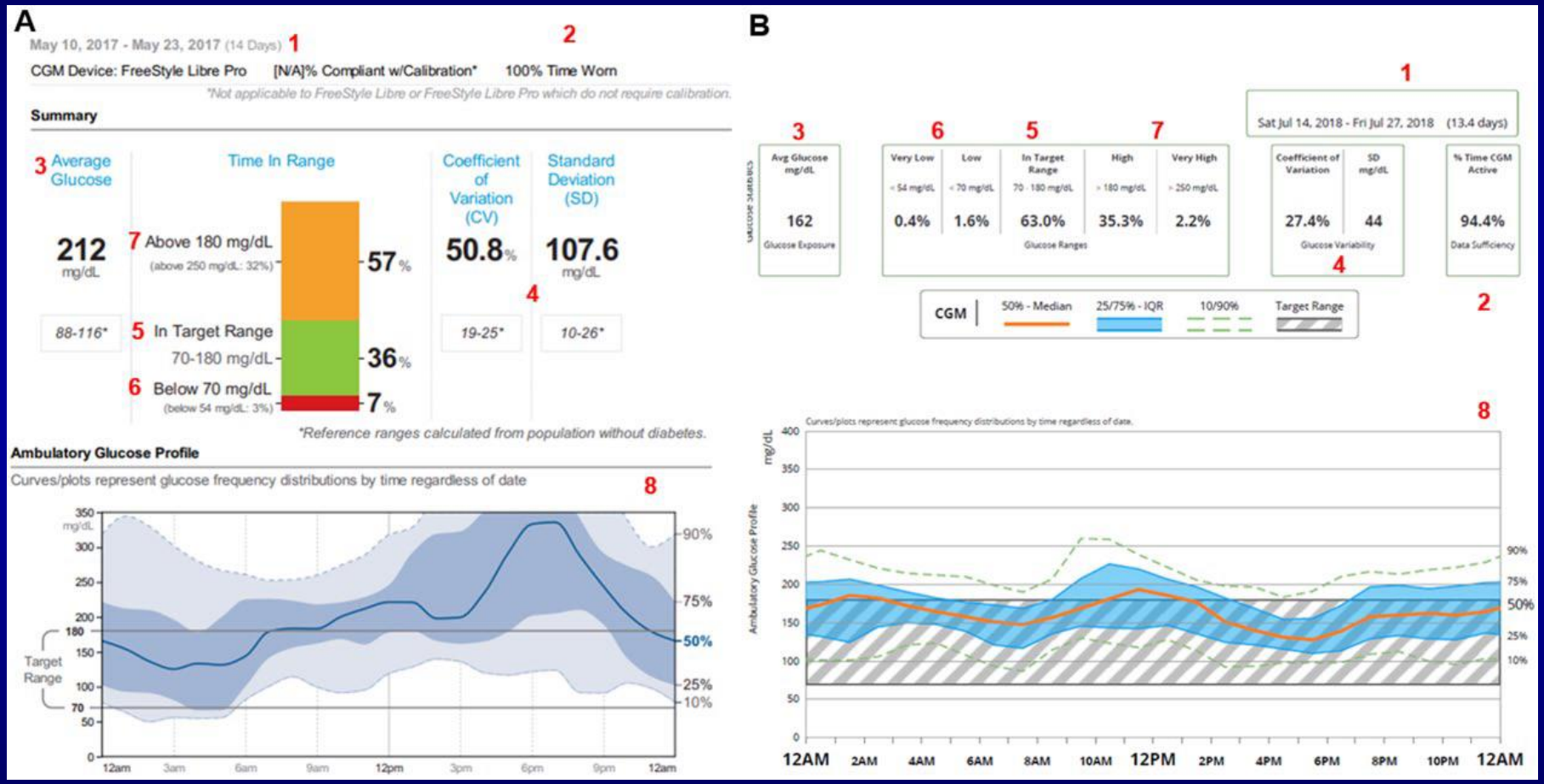
Ambulatory glucose profile (AGP)



Aleppo G, et al. J Diabetes Sci Technol 2019:13:664-673

Indications for Insulin Pump Treatment

Table 2. Indications for Insulin Pump Treatment.

• Suboptimal glycemic control in spite of efforts multiple daily insulin injections
• Frequent or unpredictable hypoglycemia and hypoglycemia unawareness
• "Dawn" phenomenon with persistent early-morning hyperglycemia
• An active lifestyle (exercise, strenuous physical activity, athletic pursuits)
• Children and young adults who typically desire fewer restrictions and more flexibility
• Growth spurt of adolescence
• Preconception planning and pregnancy
• Presence of gastroparesis
• Hectic lifestyle and frequent travel
• Shift work and erratic daily schedules
• Need for flexibility in amount and timing of meals
• Type 2 diabetes with increased insulin requirements

B McAdams, et al. Journal of Clinical Medicine 2016:5

Insulin pumps

Medtronic 770G

Tandem/Dexcom system

Omnipod/Dexcom system

Insulin pump use in T1DM

- **Basal rate: (u/hr, 47.5 units per day)**

  0000 2.05
  0430 2.00
  0700 1.85
  1400 2.00
  2000 2.10

  ICR (insulin carb ratio)
  0000 1: 8
  0500 1: 4
  1000 1: 6
  1200 1: 5
  1600 1: 3.2

  ISF (insulin sensitivity factor)
  0000 1:28
  0530 1:23
  1000 1:21
  1400 1:22

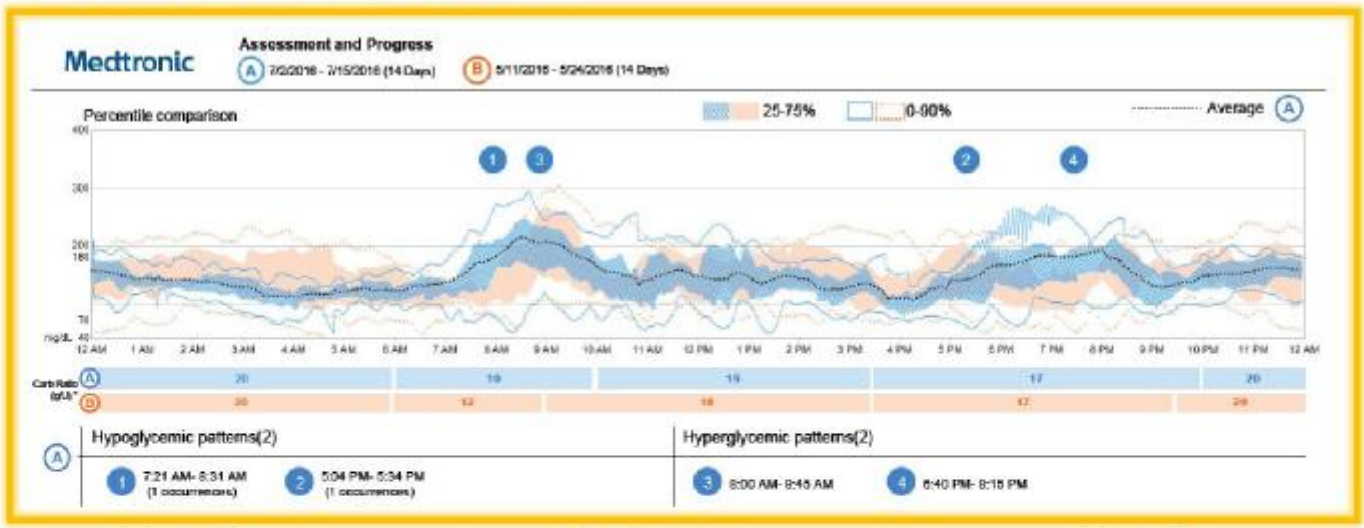
  Blood glucose target:
  0000 90-110
  0700 80-100
  2200 90-110

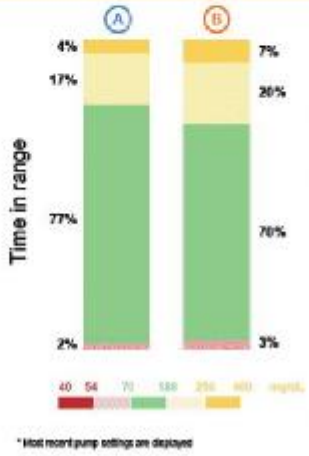
- **Active insulin time: 3 hrs**

- **Pump insulin delivery is more efficient. ~ 80% of MDI basal as a starting point.**
- **Different ICR and ISF**
- **Different BG target**

Insulin pump report

ASSESSMENT & PROGRESS REPORT





Auto Mode Exits	A	B
No Calibration	3	0
High SG Auto Mode Exit	0	0
Auto Mode max delivery	0	0
Auto Mode min delivery	0	0
BG required for Auto Mode	1	0
Sensor Algorithm Underread	0	0
Sensor Updating	0	0
No SG values	3	0
Sensor Expired	0	0
Auto Mode disabled by user	1	0
Alarms	2	0
Pump Suspend by user	0	0
Auto Mode Warm Up	0	0
Unidentified	2	2

Statistics	A	B
Auto Mode (per week)	96% (6d 18hrs)	6% (6hrs)
Manual Mode (per week)	4% (6hrs)	100% (7d 06hrs)
Sensor Wear (per week)	96% (6d 16hrs)	96% (6d 16hrs)
Average SG ± SD	149 ± 51 mg/dL	149 ± 55 mg/dL
Average BG	176 ± 74 mg/dL	147 ± 62 mg/dL
BG / Calibration (per day)	7.8 / 4.1	10.2 / 3.8
Total daily dose (per day)	23 units	18 units
Bolus amount (per day)	14U (61%)	9U (49%)
Auto Basal / Basal amount (per day)	9U (39%)	9U (51%)
Set Change	Every 4.6 days	Every 4.6 days
Reservoir Change	Every 4.6 days	Every 4.6 days
Meal (per day)	7.0	5.5
Carbs entered (per day)	166 ± 42g	148 ± 28g
Active Insulin time	3:00 hrs	3:00 hrs

Case 6

Mr. A presented to your clinic with a1c 10%. What is his estimated average glucose level?

A. 150 mg/dl

B. 240 mg/dl

C. 350 mg/dl

D. 400 mg/dl

A1c - Estimated Average Glucose

Table 6.1—Estimated average glucose (eAG)

A1C (%)	mg/dL*	mmol/L
5	97 (76–120)	5.4 (4.2–6.7)
6	126 (100–152)	7.0 (5.5–8.5)
7	154 (123–185)	8.6 (6.8–10.3)
8	183 (147–217)	10.2 (8.1–12.1)
9	212 (170–249)	11.8 (9.4–13.9)
10	240 (193–282)	13.4 (10.7–15.7)
11	269 (217–314)	14.9 (12.0–17.5)
12	298 (240–347)	16.5 (13.3–19.3)

Data in parentheses are 95% CI. A calculator for converting A1C results into eAG, in either mg/dL or mmol/L, is available at professional.diabetes.org/eAG. *These estimates are based on ADAG data of ~2,700 glucose measurements over 3 months per A1C measurement in 507 adults with type 1, type 2, or no diabetes. The correlation between A1C and average glucose was 0.92 (6,7). Adapted from Nathan et al. (6).

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Individualized Glycemic targets

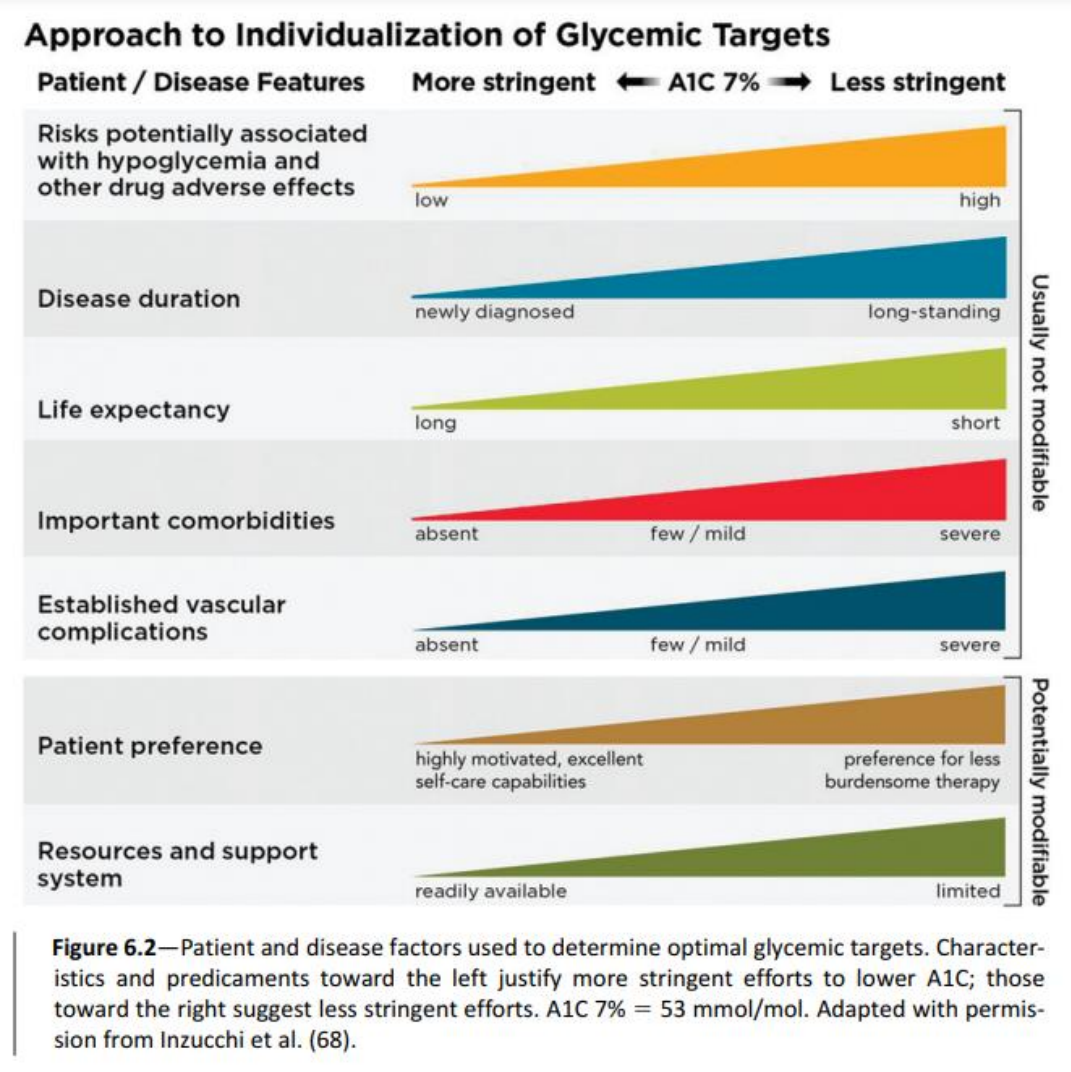

Figure 6.2—Patient and disease factors used to determine optimal glycemic targets. Characteristics and predicaments toward the left justify more stringent efforts to lower A1C; those toward the right suggest less stringent efforts. A1C 7% = 53 mmol/mol. Adapted with permission from Inzucchi et al. (68).

- **An A1c goal for many nonpregnant adults of < 7% is appropriate.**
- **Lower a1c (< 6.5%) may be acceptable if without significant hypoglycemia or other AEs of treatment.**
- **A1c goal (< 8%) may be appropriate for patients with severe hypoglycemia, limited life expectancy, advanced complications, extensive comorbid conditions or long-standing diabetes.**

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Case 7

Ms. B is a 45 yo female with T1DM for 17 years on MDI with a1c 6.2%. She was found to have hypertension with BP 150/95 mmHg. She has no history of CAD. Her urine albumin creatine ratio is normal. Which antihypertensive medications are your choices? If her urine albumin creatine ratio is 200 mg/g, which anti-hypertensive meds are your choices?

A. **Amlodipine**
B. **Lisinopril**
C. **Losartan**
D. **Chlorthalidone**

Treatment of Hypertension in people with diabetes

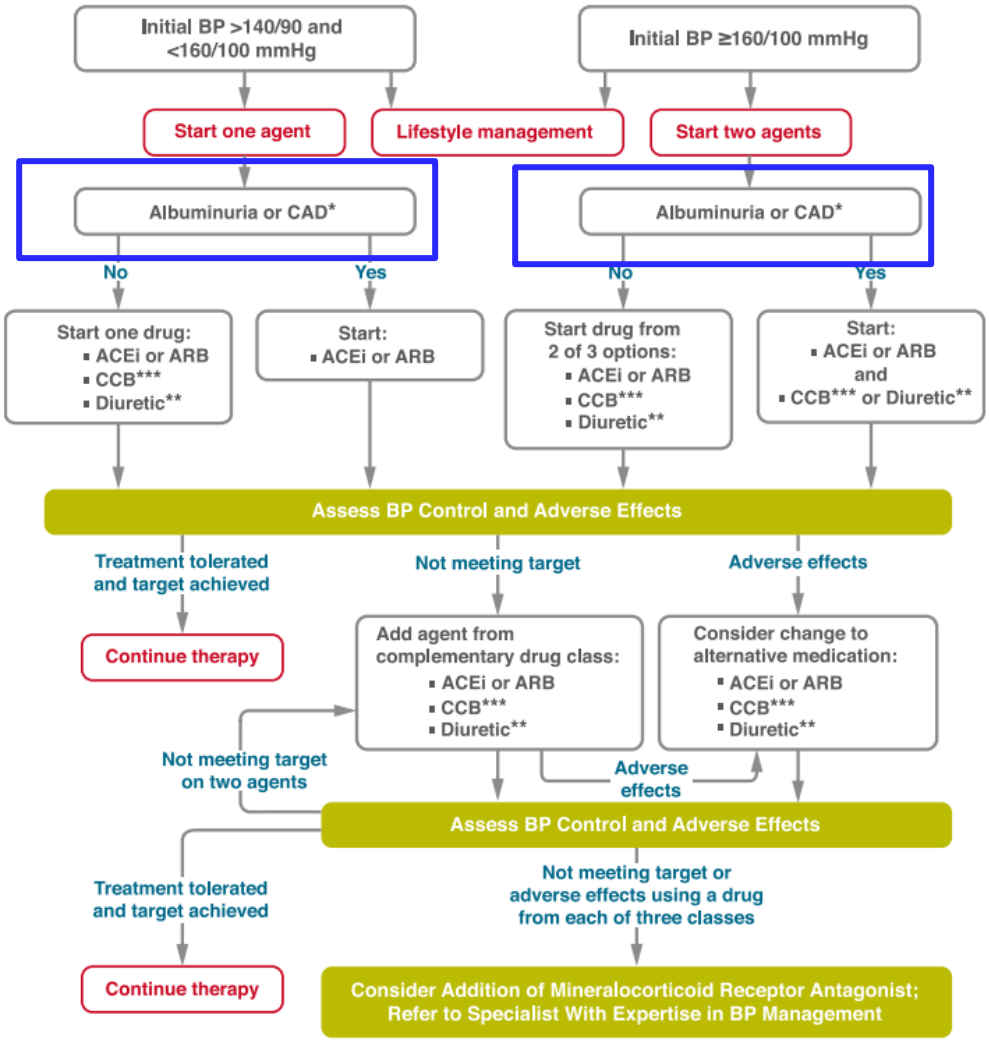

Figure 10.2—Recommendations for the treatment of confirmed hypertension in people with diabetes. *An ACE inhibitor (ACEi) or angiotensin receptor blocker (ARB) is suggested to treat hypertension for patients with coronary artery disease (CAD) or urine albumin-to-creatinine ratio 30–299 mg/g creatinine and strongly recommended for patients with urine albumin-to-creatinine ratio ≥300 mg/g creatinine. **Thiazide-like diuretic; long-acting agents shown to reduce cardiovascular events, such as chlorthalidone and indapamide, are preferred. ***Dihydropyridine calcium channel blocker (CCB). BP, blood pressure. Adapted from de Boer et al. (17).

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Management of hyperglycemic Crises

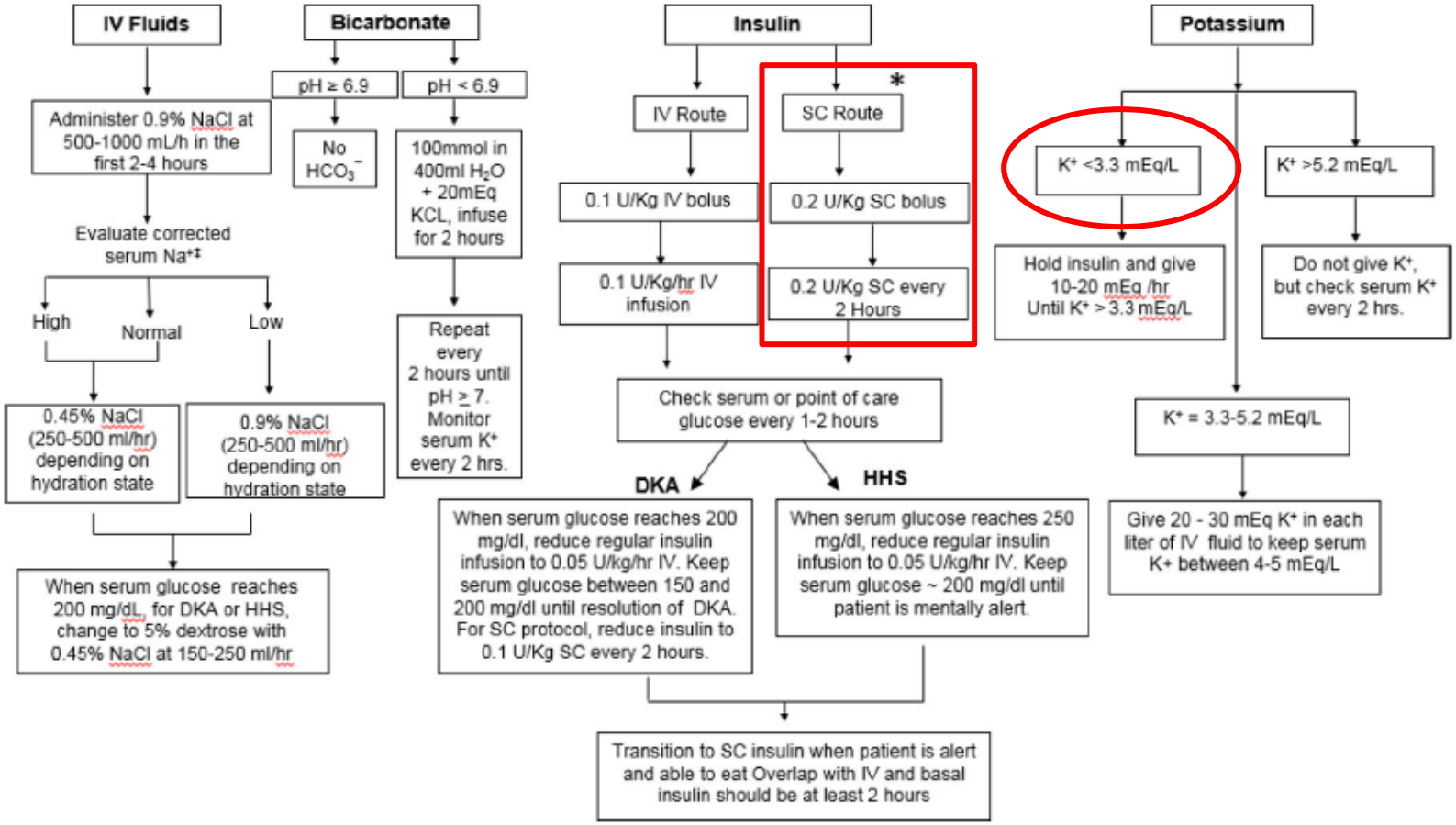


Figure 2.

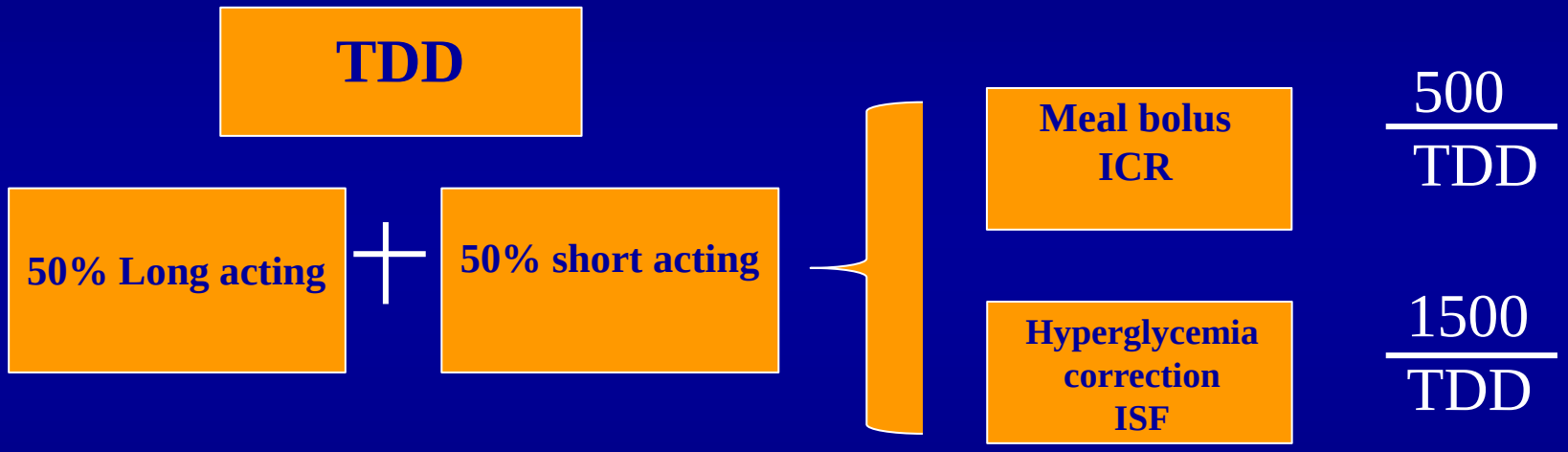
Management of Hyperglycemic Emergencies

*Subcutaneous Insulin Protocol has not been validated for HHS

Fayfman M, et al. Med Clin North Am. Management of Hyperglycemic Crises: Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar State. 2017;101(3):587-606.

Initial TDD (total daily insulin dose)

- **TDD = wt (kg) x 0.5 – T1DM, Wt (Kg) x 0.3 - pt with CKD**
- **TDD = wt (kg) x 0.7-1.0 – for obese / insulin resistant pt**



TDD = 30 units/day. ICR 1:16. ISF 1:50 over BG target
TDD = 50 units/day. ICR 1:10. ISF 1:30 over BG target
TDD = 100 units/day. ICR 1:5. ISF 1:15 over BG target

Summary

- Diagnosis of T1DM (c peptide and beta-cell autoimmune markers)
- Insulin regimen in T1DM
- New technology in T1DM including Insulin pump and CGM use
- Hyperglycemic emergency in T1DM – DKA

Q and As

Thank you !