

The Insulin Toolbox: Understanding the Options

**National Diabetes Education Program
Quarterly Webinar Series**

Tuesday, September 30, 2014
2-3 PM ET



Webinar Logistics

- All lines are muted
- Two ways to ask questions during Q&A period:
 1. Type your question into the question section and we will read your question aloud.
 2. Click the “raise hand” icon and we will call your name and unmute your line allowing you to ask your question.



Presenters

Francine R. Kaufman, M.D.

Distinguished Professor Emerita of Pediatrics and Communications, The University of Southern California and Children's Hospital Los Angeles

Chief Medical Officer and VP of Global Clinical, Medical and Health Affairs, Medtronic Diabetes

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Types of Insulins on the Market, US

- Ultra-rapid
- Short, rapid acting
- Intermediate
- Basal, long
- Mixed

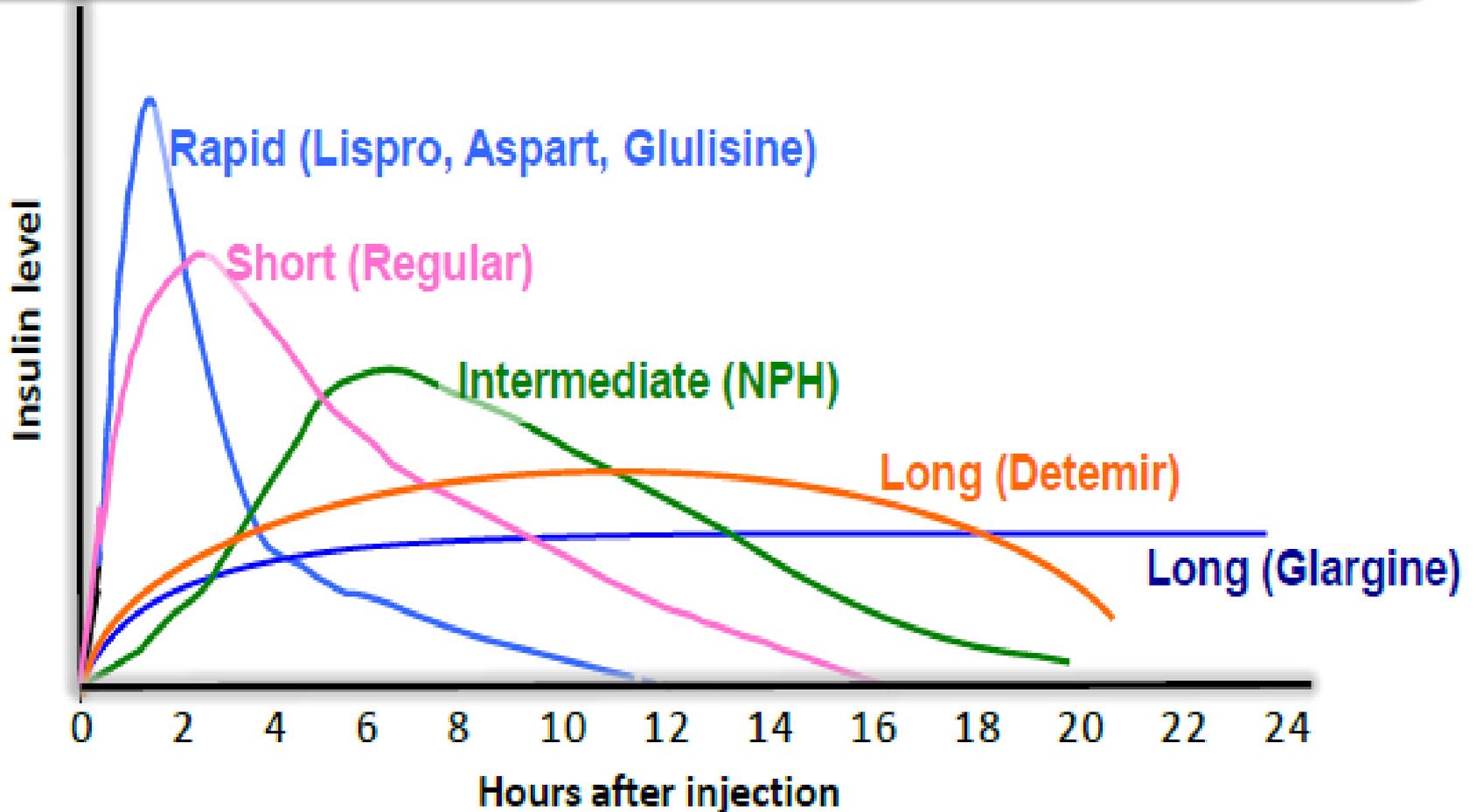


National Diabetes Education Program

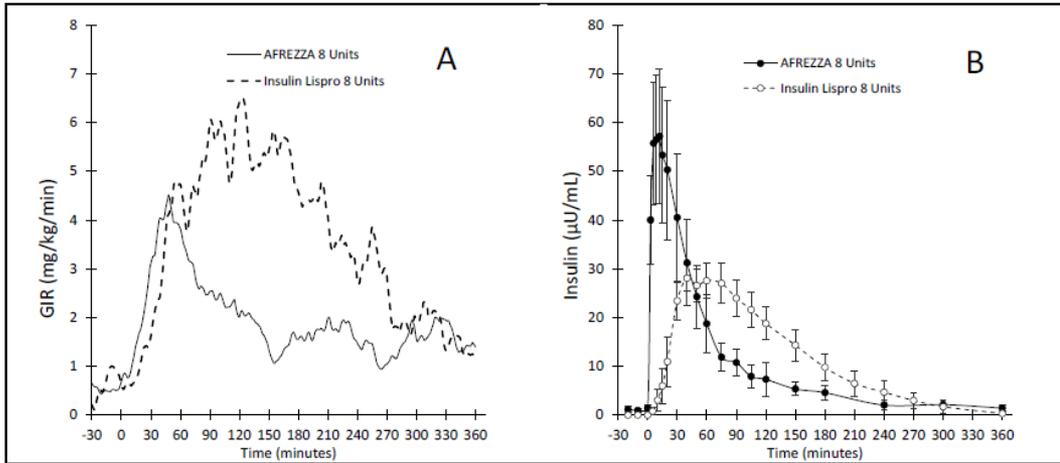
A program of the National Institutes of Health and the Centers for Disease Control and Prevention

<u>Insulin preparation</u>	<u>Onset of action</u>	<u>Peak</u>	<u>Duration of action</u>	<u>Comments</u>
<u>Rapid-acting insulin</u>				
<u>Lispro (Humalog)</u>	5 to 15 minutes	1 to 2 hours	4 to 5 hours	—
<u>Aspart (Novolog)</u>	5 to 15 minutes	1 to 2 hours	4 to 5 hours	—
<u>Glulisine (Apidra)</u>	5 to 15 minutes	1 to 2 hours	4 to 5 hours	—
Regular (recombinant) (Humulin R)	30 to 60 minutes	2 to 4 hours	8 to 10 hours	Inject 30 minutes before meal
<u>Intermediate-acting insulin</u>				
<u>Isophane (NPH) (Humulin, Novolin N)</u>	1 to 2 hours	4 to 8 hours	10 to 20 hours	—
<u>Basal insulin</u>				
<u>Detemir (recombinant) (Levemir)</u>	1 to 2 hours	Relatively flat	12 to 20 hours	Smoother curve than NPH; administered 1-2/d; pen form; without refrigeration up to 42 d
<u>Glargine (Lantus)</u>	1 to 2 hours	Relatively flat	20 to 24 hours	Available in pen form
<u>Mixed insulin</u>				
Multiple preparations (e.g., Humulin 70/30)	30 minutes	Dual peak	Up to 24 hours	Mixed insulin preparations may hinder tight glycemic control

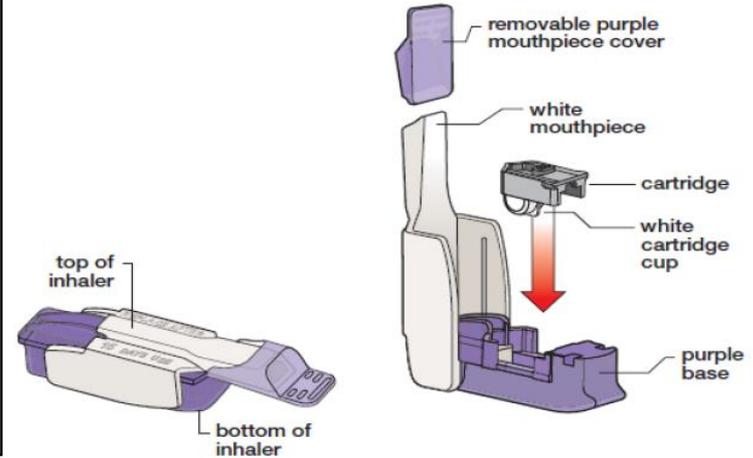
Insulin Profiles



Afrezza® Inhaled Human Insulin



* Despite the faster absorption of insulin (PK) from Afrezza, the onset of activity (PD) was comparable to insulin lispro.



Efficacy Parameter	Afrezza + OAD N= 177	Placebo + OAD N= 176	Confidence Interval
Change in HgbA1c (%)	-0.82	-0.42	(-0.57, -0.23)
% Patients achieving HgbA1c ≤ 7%	32.2	15.3	-

Efficacy Parameter	Inhaled insulin + basal insulin n = 174	Insulin aspart + basal insulin n = 170	Confidence Interval
Change in HgbA1c (%)	-0.21	-0.4	(-0.57, -0.23)
% Patients achieving HgbA1c ≤ 7%	13.8	27.1	-



New Insulin Products on the Horizon

- New basal, longer acting
 - Reduce hypo and hyperglycemia
- Ultra-rapid insulin
 - Improve post meal hyperglycemia
 - Use in artificial pancreas systems
- Bio-engineered, “biosimilars”
 - Reduce cost
- Concentrated insulin
 - Inject less often
 - Reduce cost?



Methods of Insulin Delivery

- Syringes
- Pens
- Pumps
 - Artificial pancreas systems
- Inhaled
- Oral, Buccal, Intradermal
- Intraperitoneal
 - Through pump or peritoneal catheter
- Smart insulin



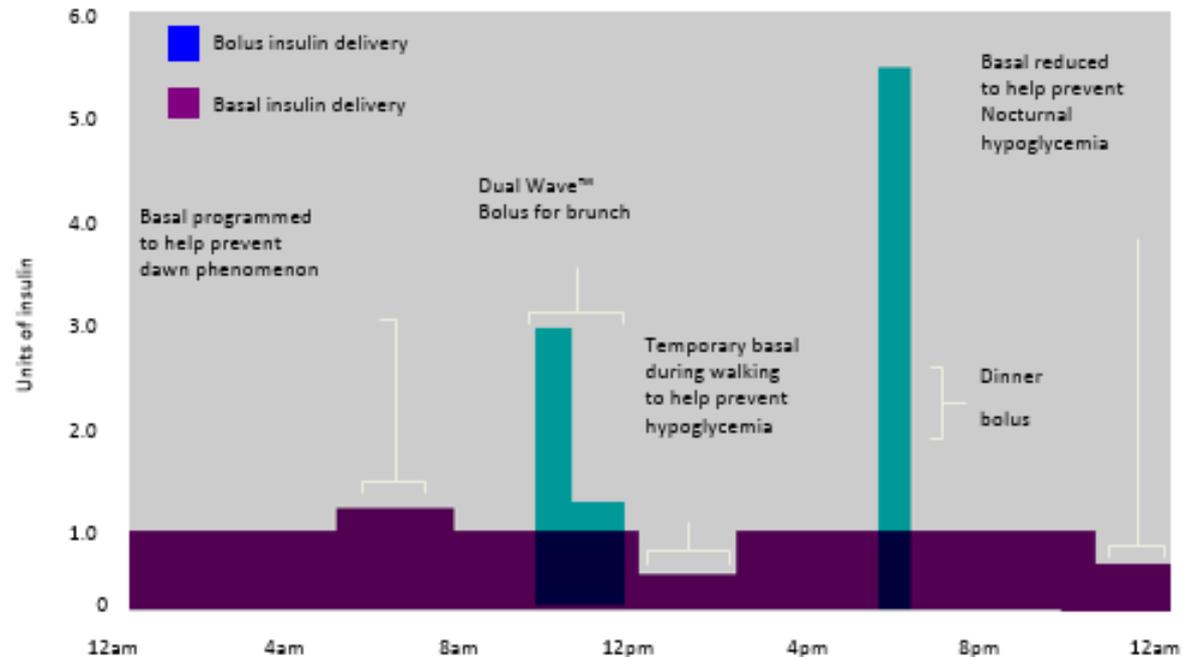
Insulin Pens

- More discreet
- Combines insulin container and syringe into a single modular unit
- More convenient than carrying insulin vials and syringes
- More accurate
 - Insulin-dose setting dial, audible clicks
- High patient satisfaction



Insulin Pumps

- Delivery is customizable, flexible, adjustable, precise and reproducible
- Uses only rapid insulin with less variability in absorption
- Advanced features – dosage calculators, integrated with CGM, suspend feature
- Durable, patch





ADA Standards of Care

Glycemic Targets Differ by Age, Patient Characteristics

- Glycemic targets used to be fixed
- Now by age and patient characteristics
- Pediatrics - <7.5%
- Adult if possible <7%
- If Issues:
- Avoid fixed insulin regimens
- 3-4 injections of basal and prandial insulin or CSII (grade of evidence, A)
- Match prandial insulin dose to carbohydrate intake, pre-meal glucose and anticipated activity (grade of evidence, E)
- Use insulin analogs (grade of evidence, A)

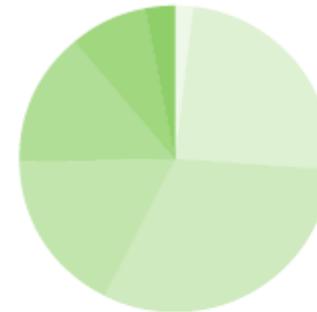
Patient characteristics/ health status	Rationale	Reasonable A1C goal‡	Fasting or preprandial glucose (mg/dL)	Bedtime glucose (mg/dL)	Blood pressure (mmHg)	Lipids
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.5%	90–130	90–150	<140/80	Statin unless contraindicated or not tolerated
Complex/intermediate (multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild-to-moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0%	90–150	100–180	<140/80	Statin unless contraindicated or not tolerated
Very complex/poor health (long-term care or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or 2+ ADL dependencies)	Limited remaining life expectancy makes benefit uncertain	<8.5%†	100–180	110–200	<150/90	Consider likelihood of benefit with statin (secondary prevention more so than primary)



The Type 1 Exchange – Real Life US Type 1 Diabetes Data from the 2013 Annual Report

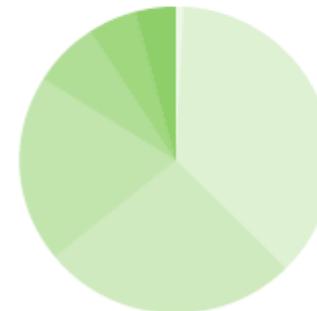
- 26,293 participants
- 73 sites
- 59% use insulin pump therapy, CSII
- 41% use multiple daily injections, MDI

Current age



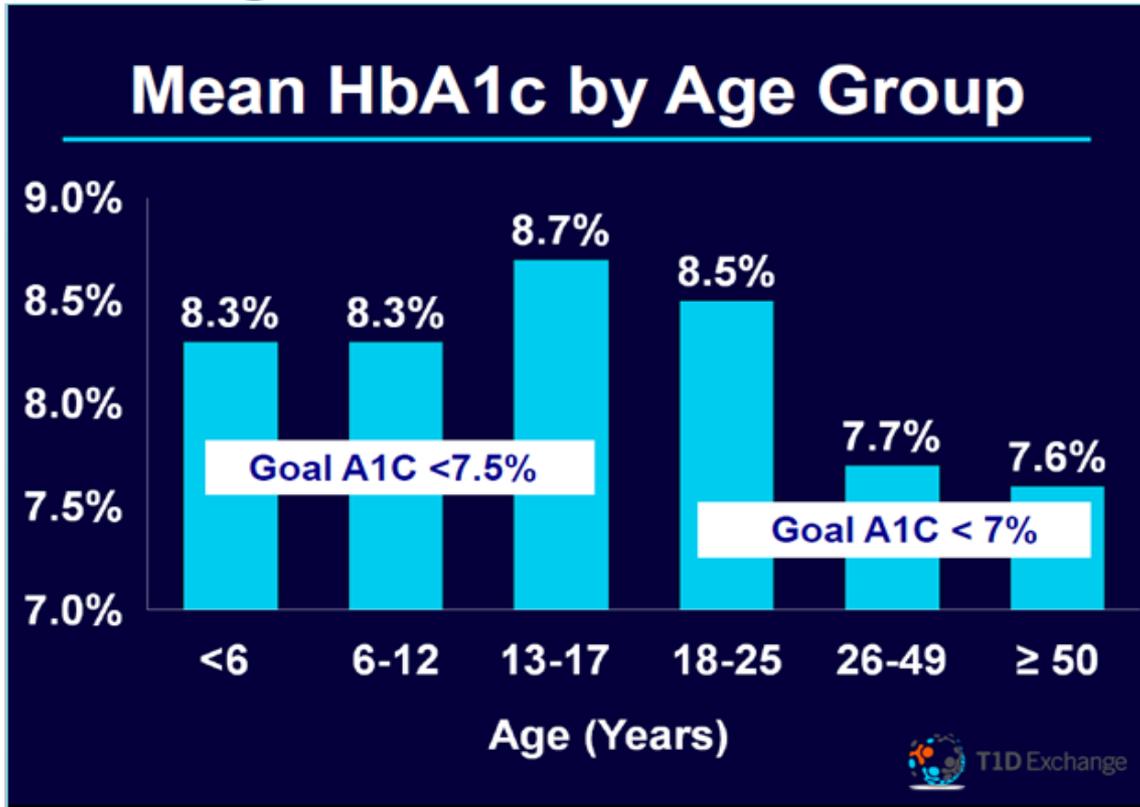
2%	<6 years
24%	6–<13 years
31%	13–<18 years
17%	18–<26 years
14%	26–<50 years
8%	50–<65 years
3%	≥65 years

Current T1D duration



<1%	1 year
37%	1–5 years
27%	6–10 years
20%	11–20 years
7%	21–30 years
5%	31–40 years
4%	≥41 years

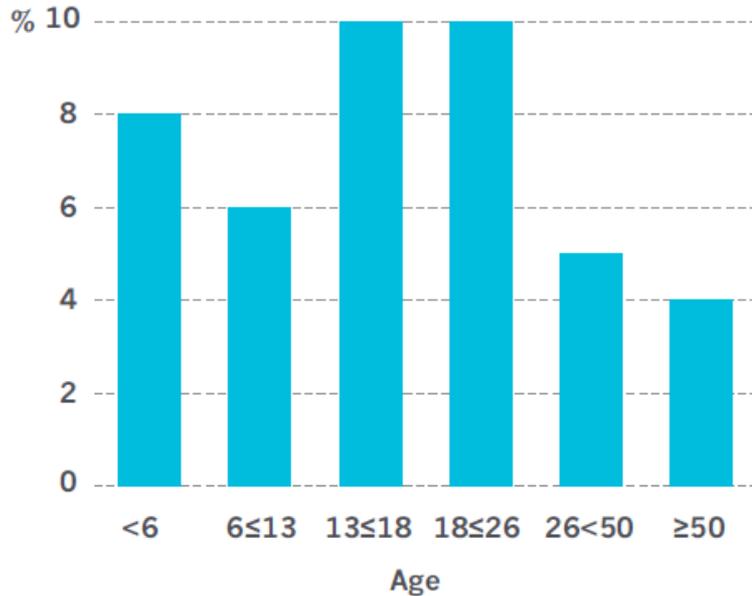
The Type 1 Exchange Data Shows Target A1C Not Achieved





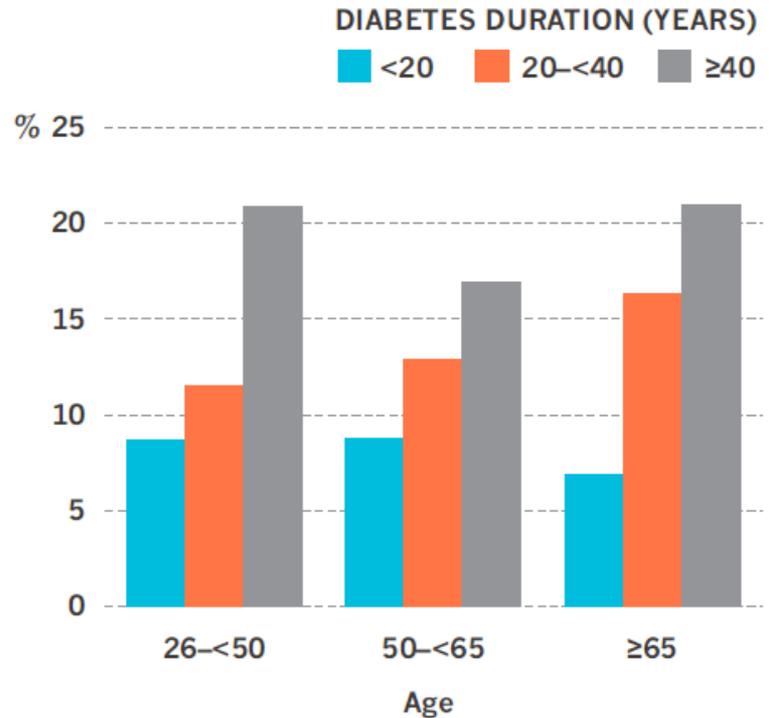
Unacceptable Rates of DKA and Severe Hypoglycemia

12-month frequency of diabetic ketoacidosis* according to age



*1 or more events in 12 mo

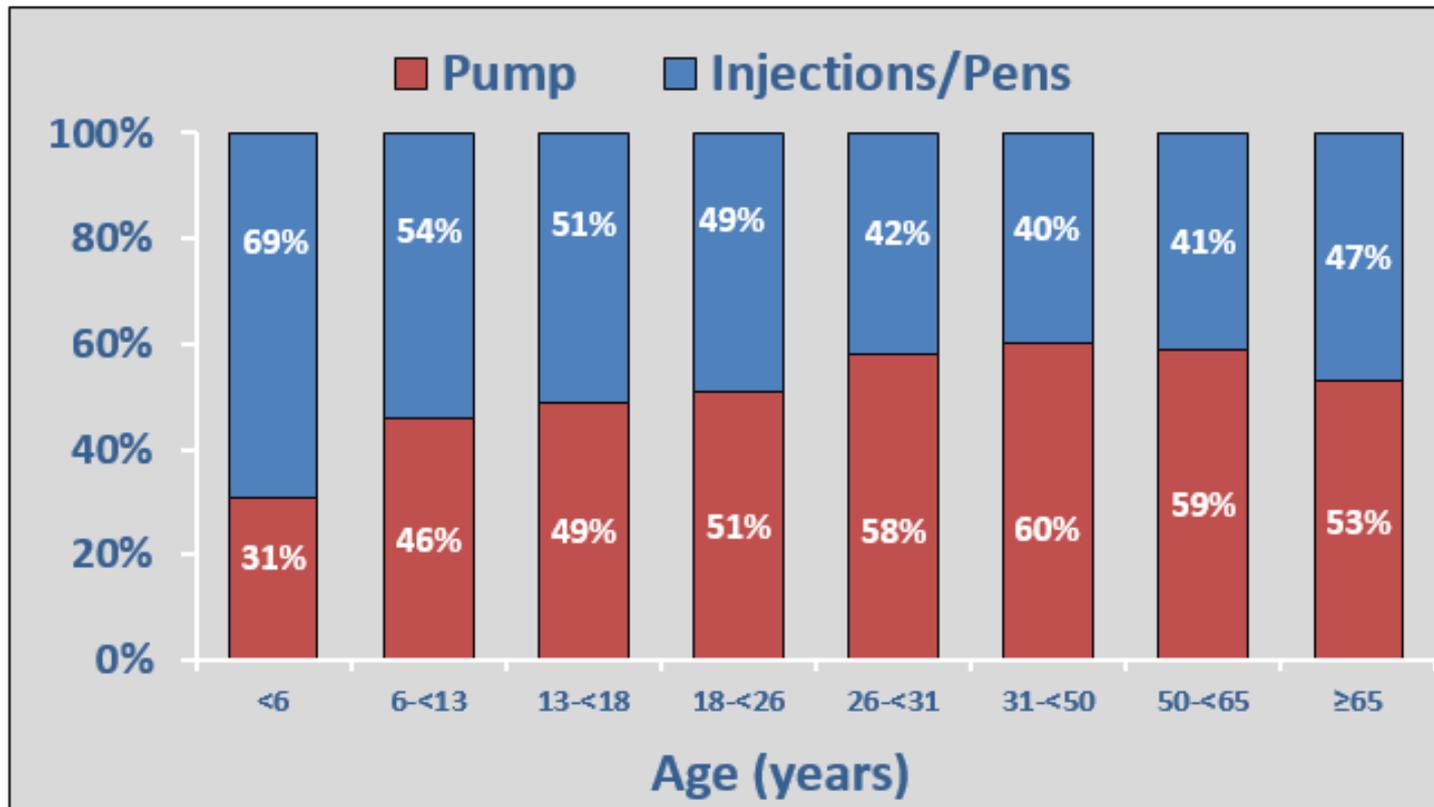
12-month frequency of severe hypoglycemia*



*1 or more events in 12 mo

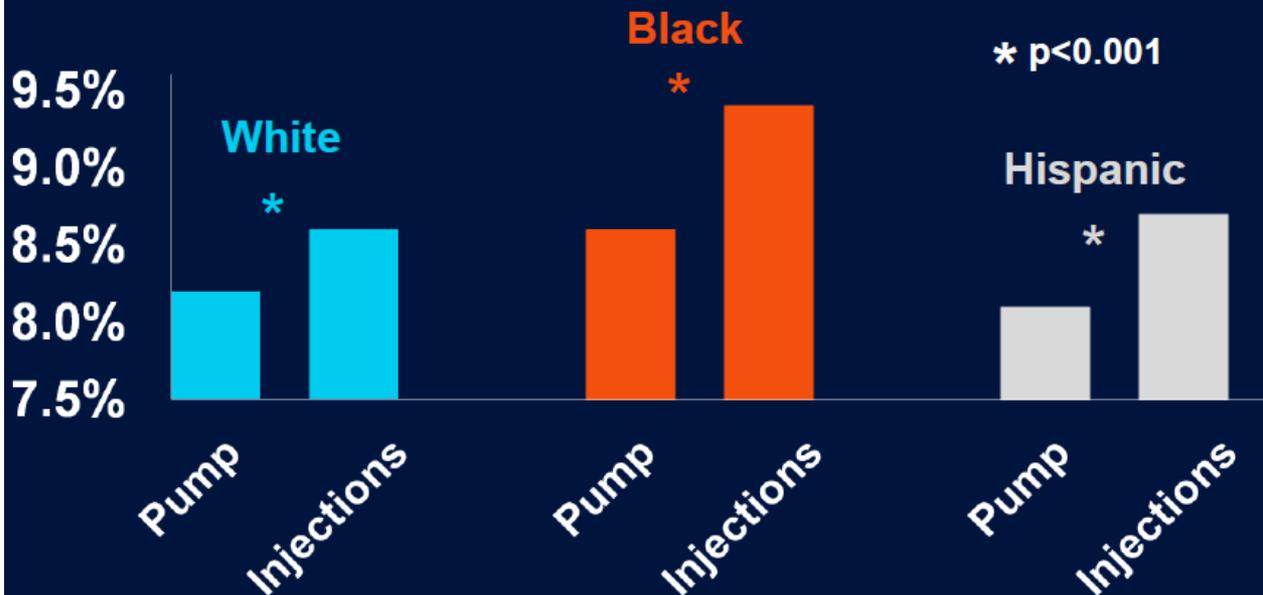


Insulin Delivery Method in the Type 1 Exchange By Age



Insulin Delivery Method in the Type 1 Exchange By Race/Ethnicity and A1C Outcomes

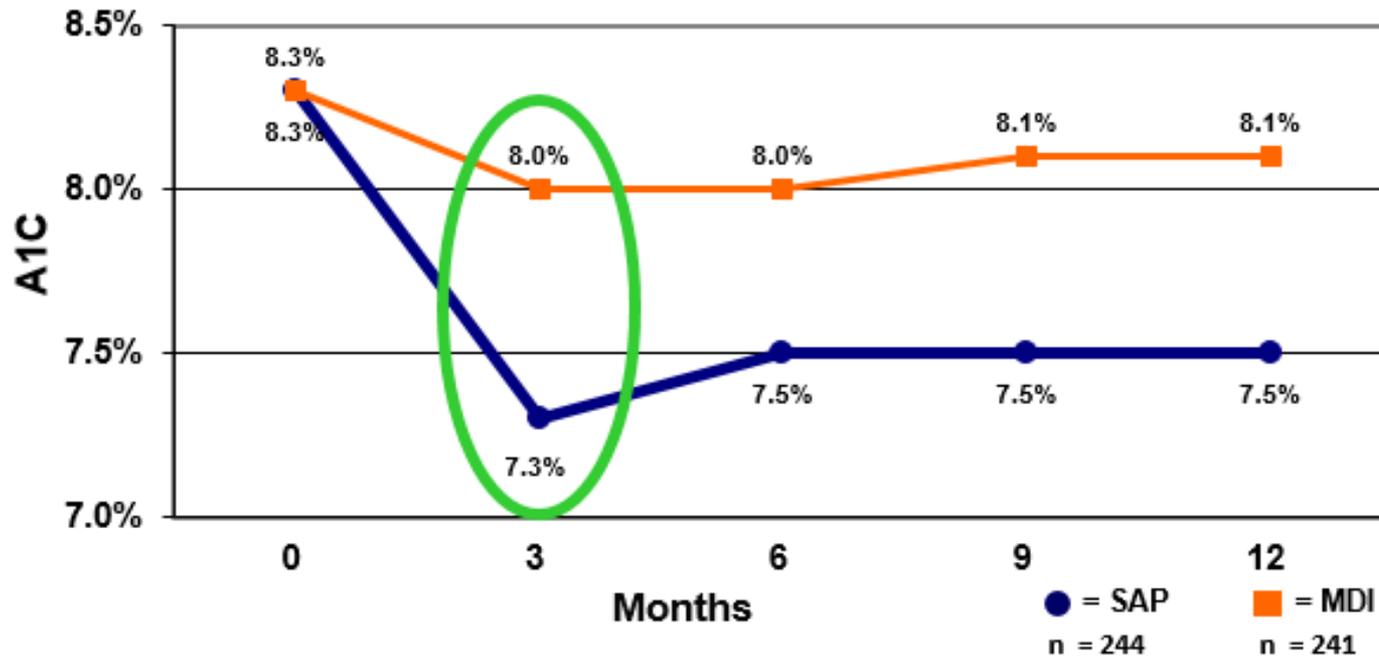
HbA1c according to Insulin Method Stratified by Race/Ethnicity



*Means and P value adjusted for confounders

Insulin Pump Combined with Continuous Glucose Monitor Improved A1C Outcome without Increasing Hypoglycemia

A1C Reduction for SAP and MDI Groups



Values are means \pm SE. Comparisons between SAP group and MDI group are significant for each time period ($P < 0.001$).

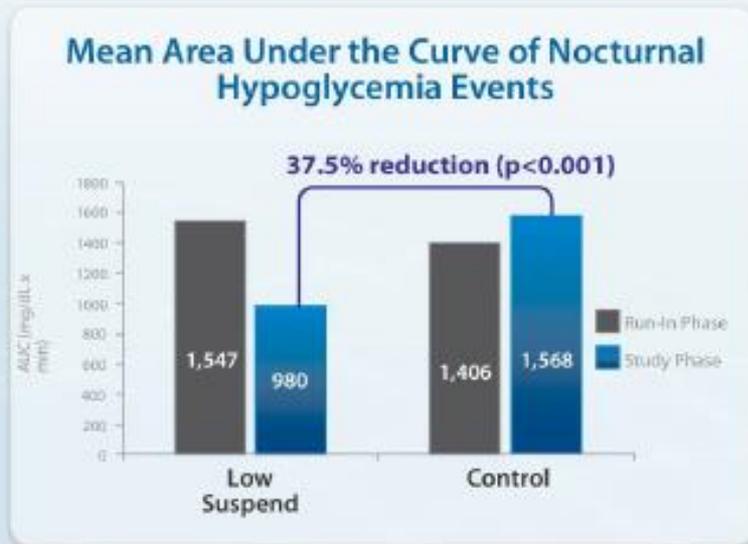


The Suspend Feature of the Sensor-Augmented Pump

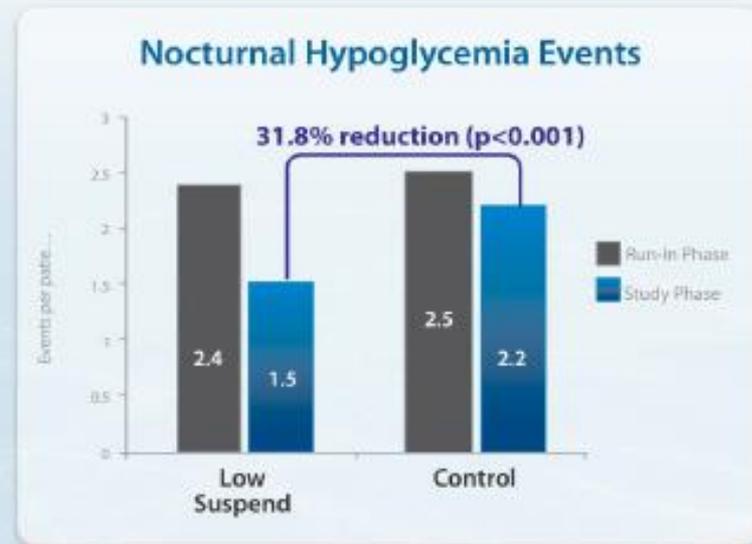
In the ASPIRE In-Home study, the MiniMed™ sensor-augmented insulin pump with low suspend feature prevented more nocturnal hypoglycemic events than an insulin pump without that feature. (n=247, age 16 to 70 years)

Bergenstal RM, Klonoff DC, Bode BW, et al. Threshold-based insulin-pump interruption for reduction of hypoglycemia. *N Engl J Med.* 2013;369(3):224-232.

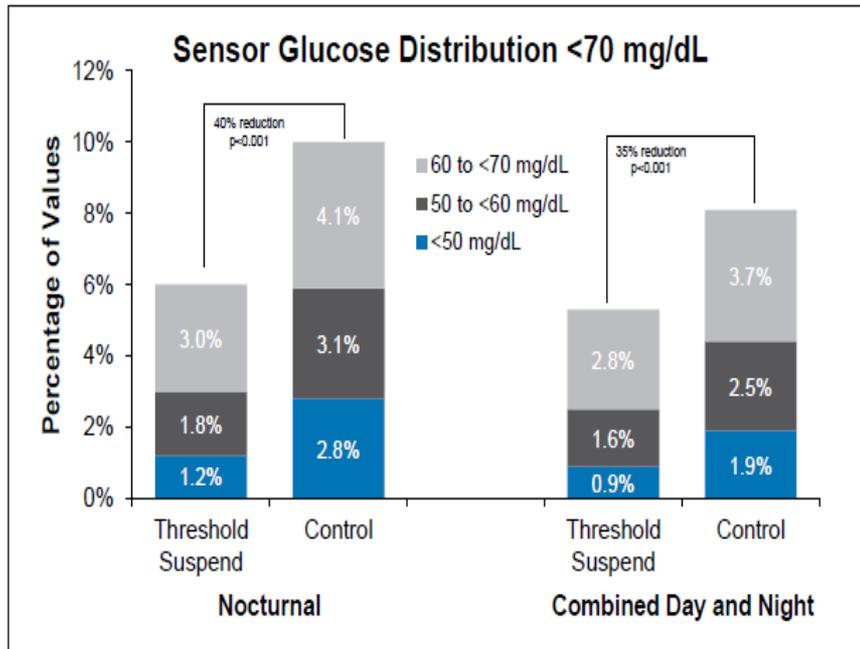
37.5% reduction in the combined magnitude and duration of nocturnal hypoglycemia events.



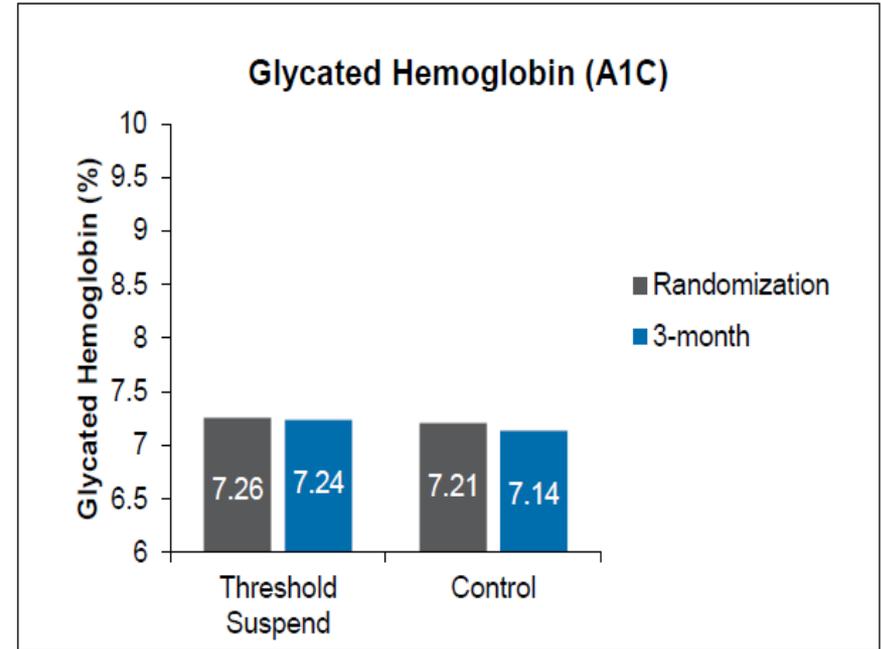
31.8% fewer nocturnal hypoglycemic events.



Clinical Evidence for Suspend Feature: *ASPIRE In-Home*



There were fewer SG values in hypoglycemic ranges in the Threshold Suspend Group.



Δ A1C was similar in the two groups. The 95% CI of the difference in Δ A1C (-0.05, 0.15) did not include the non-inferiority limit of 0.4%.

Study conducted with Veo pump. Not FDA approved and not commercially available in the US.

Bergenstal RM, Klonoff DC, Garg SK, et al. Threshold-based insulin-pump interruption for reduction of hypoglycemia. *N Engl J Med*. 2013 June 22;DOI: 10.1056/NEJMoa1303576.



Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach

Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

1. Patient-Centered Approach

"...providing care that is respectful of and responsive to individual patient preferences, needs, and values - ensuring that patient values guide all clinical decisions."

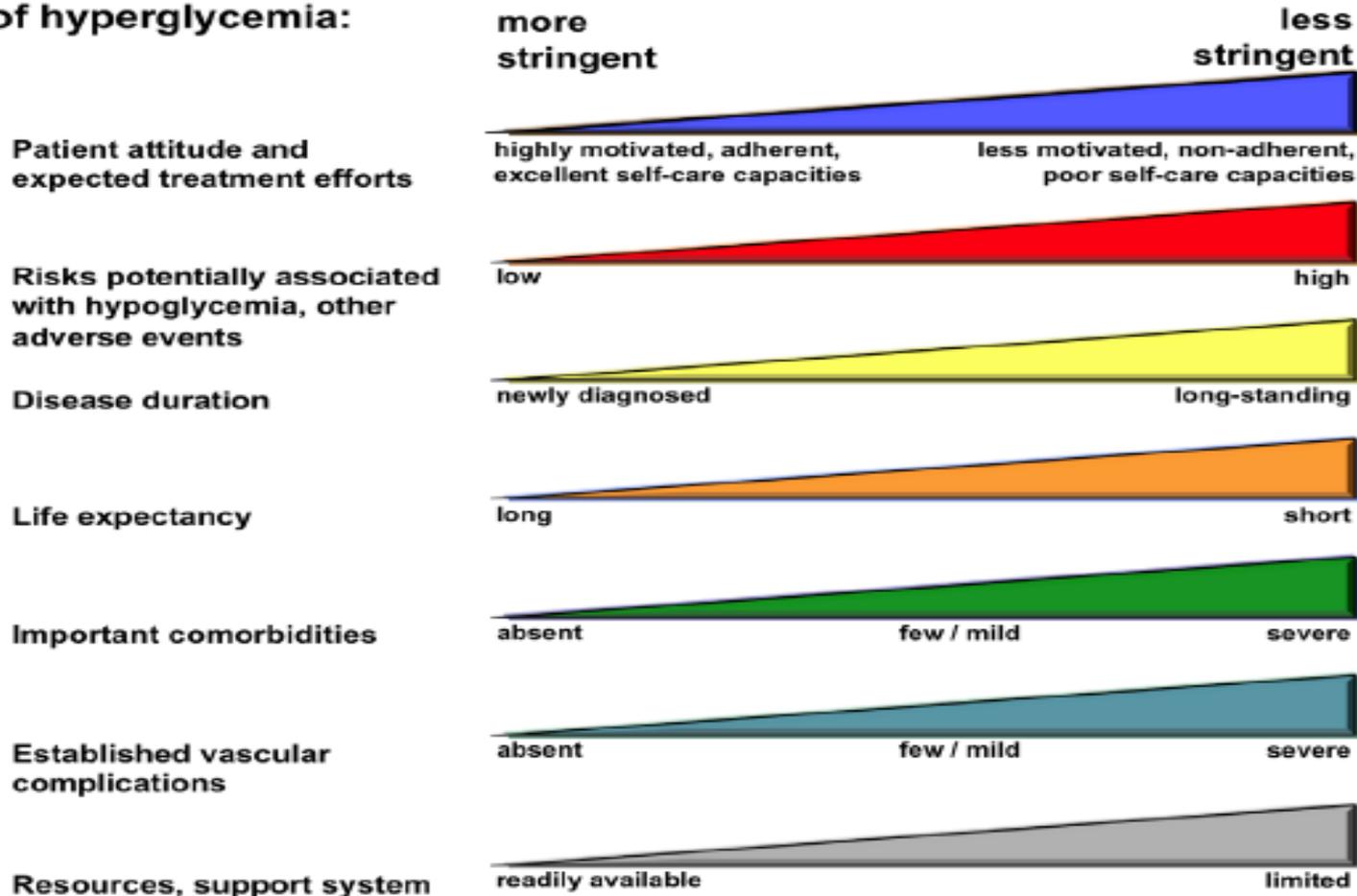
- Gauge patient's preferred level of involvement.
- Explore, where possible, therapeutic choices.
- Utilize decision aids.
- Shared decision making – final decisions re: lifestyle choices ultimately lies with the patient.





Approach to Management of Hyperglycemia

Approach to management of hyperglycemia:





Initial drug monotherapy

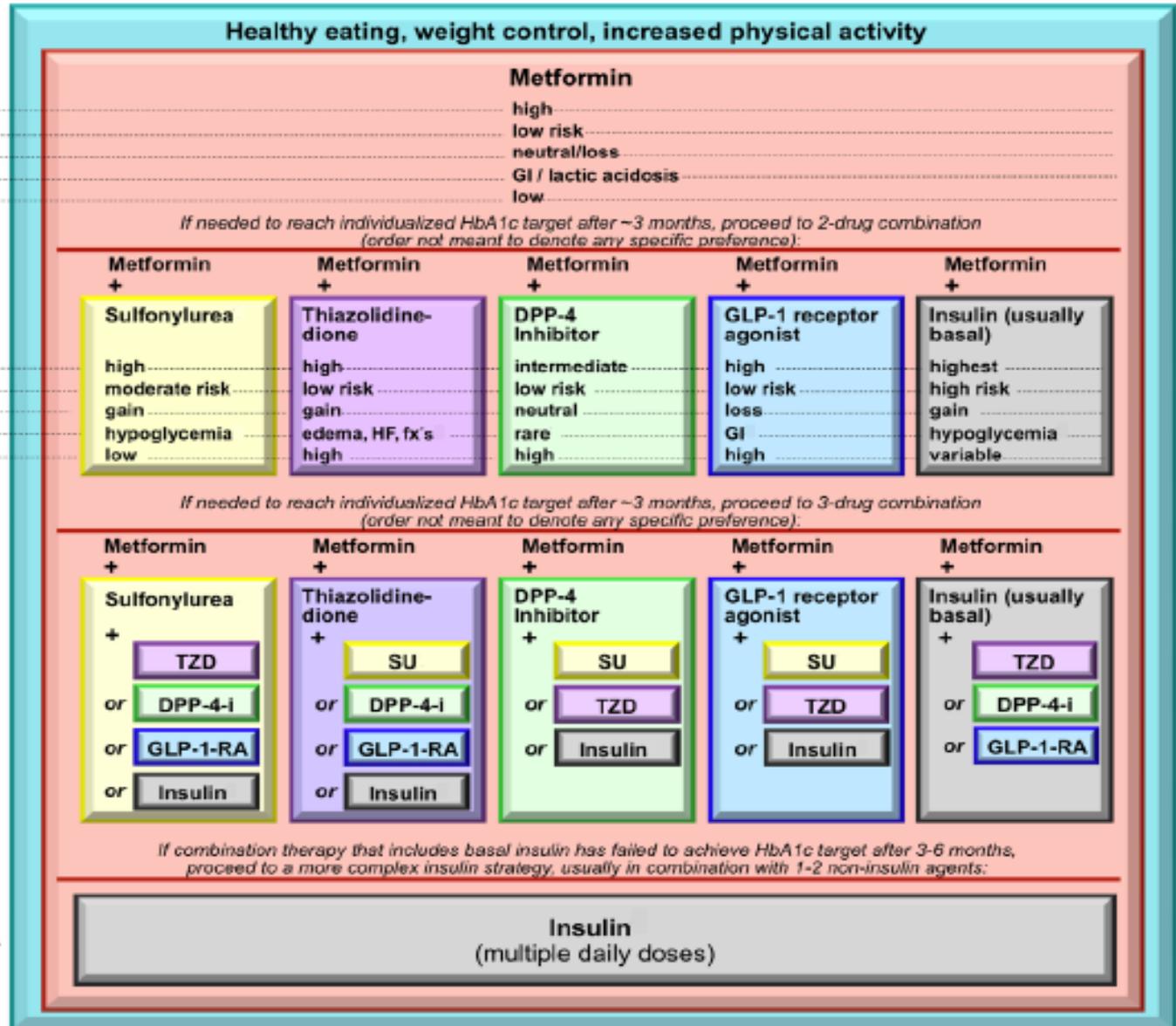
- Efficacy (↓ HbA1c)
- Hypoglycemia
- Weight
- Side effects
- Costs

Two drug combinations

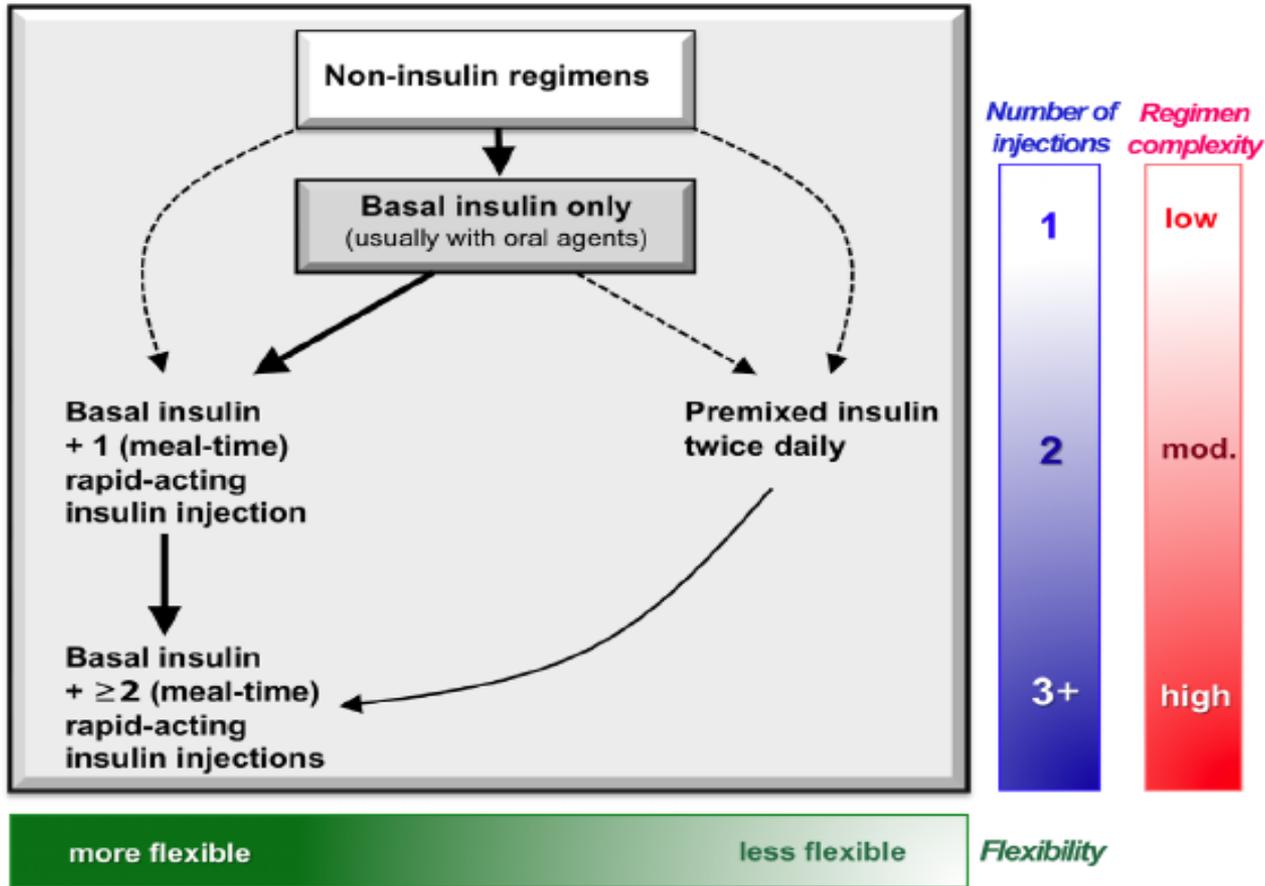
- Efficacy (↓ HbA1c)
- Hypoglycemia
- Weight
- Major side effect(s)
- Costs

Three drug combinations

More complex insulin strategies



Insulin Regimens in Type 2 Diabetes





ALGORITHM FOR ADDING/INTENSIFYING INSULIN

Copyright © 2013 AAACE AAACE Comprehensive Diabetes Management Algorithm, *Endocr Pract.* 2013;19(No. 2) 333

START BASAL (long-acting insulin)

A1c < 8%

TDD
0.1–0.2 U/kg

A1c > 8%

TDD
0.2–0.3 U/kg

Insulin titration every 2–3 days to reach glycemic goal:

- Fixed regimen: Increase TDD by 2 U
- Adjustable regimen:
 - **FBG** > 180 mg/dL: add 4 U
 - **FBG** 140–180 mg/dL: add 2 U
 - **FBG** 110–139 mg/dL: add 1 U
- If hypoglycemia, reduce TDD by:
 - **BG** < 70 mg/dL: 10% – 20%
 - **BG** < 40 mg/dL: 20% – 40%

Consider discontinuing or reducing sulfonylurea after basal insulin started (basal analogs preferred to NPH)

** Glycemic Goal:

- For most patients with T2D, an A1c < 7%, fasting and premeal **BG** < 110 mg/dL in the absence of hypoglycemia.
- A1c and **BG** targets may be adjusted based on patient's age, duration of diabetes, presence of comorbidities, diabetic complications, and hypoglycemia risk.

Glycemic Control
Not at Goal**

INTENSIFY (prandial control)

Add GLP-1 RA
or DPP4-i

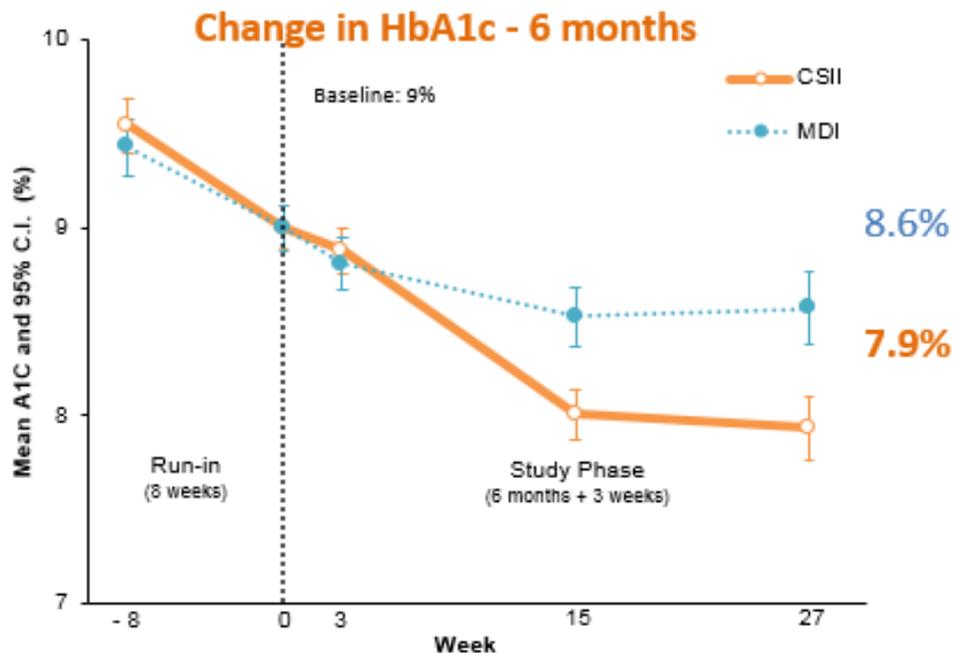
Add Prandial Insulin

TDD: 0.3–0.5 U/kg
50% Basal Analog
50% Prandial Analog
Less desirable: NPH
and regular insulin or
premixed insulin

Insulin titration every 2–3 days to reach glycemic goal:

- Increase basal TDD as follows:
 - Fixed regimen: Increase TDD by 2 U
 - Adjustable regimen:
 - **FBG** > 180 mg/dL: add 4 U
 - **FBG** 140–180 mg/dL: add 2 U
 - **FBG** 100–139 mg/dL: add 1 U
- Increase prandial dose by 10% for any meal if the 2-hr postprandial or next premeal glucose is > 180 mg/dL
- Premixed: Increase TDD by 10% if fasting/premeal **BG** > 180 mg/dL
- If fasting AM hypoglycemia, reduce basal insulin
- If nighttime hypoglycemia, reduce basal and/or pre-supper or pre-evening snack short/rapid-acting insulin
- If between meal daytime hypoglycemia, reduce previous premeal short/rapid-acting insulin

CSII Compared to MDI in Type 2 Diabetes Patients Not at Target with MDI – Global OpT2mise Trial



A 6-month randomized controlled trial, N=495 adults entered the run-in study phase. With a 6-month extension period.

Reduction of HbA1c :

CSII group : -1.1%
(HbA1c drop from 9.0% to 7.9%)

MDI group: -0.4%
(HbA1c drop from 9.0% to 8.6%)

A difference of 0.7% in favor of CSII group (p<0.001)

Insulin pump therapy (CSII) significantly improved glycemic control compared to multiple daily injections



Key Points of ADA/EASD Type 2 Approach

- Individualized glycemic targets and BG lowering therapies
- Diet, education and exercise are the foundation
- Unless contraindicated, metformin is optimal first-line drug
- After metformin, combination therapy with 1-2 other oral / injectable agents is reasonable, minimize side effects
- Ultimately, many patients will require insulin therapy alone or in combination with other agents
- All treatment decisions should be made in conjunction with the patient – focus on preferences, needs and values
- Comprehensive CV risk reduction should be a major focus



Provider Barriers that Delay Insulin

- Stepwise "treatment to failure" approach
- Lack of consensus regarding treatment goals and the best practices
- Clinical inertia
- Propensity to delay, until "absolutely necessary"
- Lack of access to team for education and support
 - Underutilization of diabetes education
 - Lack of access (i.e., in rural areas)
 - Inadequate reimbursement
 - Physician unawareness of diabetes education resources



Barriers to Optimal Care – Patient Delay Insulin or Interfere with Adherence

Educational

- Low diabetes knowledge
- Low knowledge of services

Internal physical

- Physical effects of treatment

External physical (systems)

- Personal finance issues
- Poor physical access to service
- Limited range of services
- Poor quality of services
- Lack of community-based services
- Need for more helpful health professionals
- Inappropriate diabetes care

Psychosocial

- Group pressure
- Prejudice
- Lack of public awareness
- Lack of family support
- Family demands
- Lack of community support
- Communication difficulties
- Lack of cultural support

Psychological

- Health beliefs
- Public health beliefs
- Poor motivation
- Low self-efficacy
- No symptom cues
- Difficulty setting priorities
- Negative perceptions of time
- Emotional issues
- Precontemplative stage of change

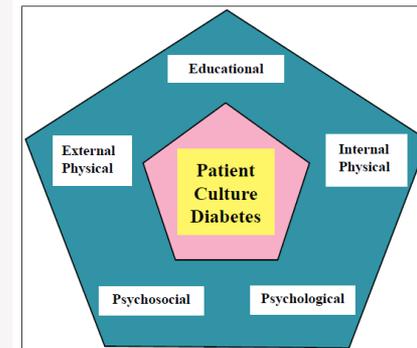


Figure 1. Personal barriers to diabetes care



Recommendations for the Provider to Enhance Advancement and Adherence to Use of Insulin

- Consider cultural issues, ask what's important to the patient
- Enhance DSME – diabetes education
- Co-manage with a team
- Refer to social workers, mental health
- Help with financial issues, co-pays, insurance
- Alter insulin dosage as needed, ask about side effects
- Encourage and support glucose monitoring
- Believe in the patient, meet them where they are



Cases 1

- 22 year old female with BMI 28 kg/m², develops of polyuria, weight loss, polydipsia during graduate school
- Goes to health center, BG 218 mg/dL after lunch
 - Repeat glucose – fasting 189 mg/dL
- What do you do?
- Do you think she will need insulin? (Yes or No)



Case 1

- GAD auto-antibodies come back positive
- What regimen do you start her on?
 - A. Fixed 2 shots of premix AM and PM
 - B. Basal plus prandial insulin for carbohydrate counting
 - C. Basal plus prandial insulin for fixed meals
 - D. Basal only at night



Case 1

- 1 year later her A1C is 7.8% and her meter download shows mean glucose of 175 mg/dL, Standard deviation of 98 mg/dL, 12% low glucose and 38% high glucose values.
- She had a fender bender due to low glucose. What do you consider?
 - A. Get her license revoked
 - B. Insulin pump therapy
 - C. Diabetes education, review correcting highs and carb counting
 - D. Pump and sensor with threshold suspend
 - E. Counsel her to check glucose before driving



Case 2

- A 56 year old man was diagnosed with type 2 diabetes at age 42 years when his BMI was 35 kg/m²
- At diagnosis, he was placed on diet and exercise
- At 3 months, A1C was 9.8%, started metformin, then A1C in low 8 range
- At 5 years, A1C > 9.0%, BMI increased to 37 kg/m², added second oral, then A1C is mid 8 range
- At 10 years, A1C > 9.0%, added 3rd oral, then A1C in mid-to-high 8 range
- At 14 years, A1C > 9.0%
- What would you do?



Case 2

- What would you do?
 - A. Change oral agents
 - B. Add basal insulin
 - C. Add prandial insulin
 - D. Go to MDI regimen



Case 2

- You begin basal insulin at night
- What do you do?
 - A. Teach how to count carbohydrate
 - B. Educate about recognizing and treating hypoglycemia
 - C. BG monitoring not important without prandial insulin
 - D. Continue 3 oral medications

Related Resources from NDEP and Partner Organizations

Joanne Gallivan, M.S., R.D.

Director, National Diabetes Education Program
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health



A program of the National Institutes of Health and the Centers for Disease Control and Prevention





National Diabetes Education Program

A program of the National Institutes of Health and the Centers for Disease Control and Prevention

Related NDEP Resources

www.YourDiabetesInfo.org/Publications

Know Your Blood Sugar Numbers

If you have diabetes, keeping your blood sugar (glucose) numbers in your target range can help you feel good today and stay healthy in the future.

NDEP National Diabetes Education Program
A program of the National Institutes of Health and the Centers for Disease Control and Prevention

Conozca sus niveles de azúcar en la sangre

Si usted tiene diabetes, mantener el nivel de azúcar en la sangre (glucosa) dentro de su rango meta le puede ayudar a sentirse bien hoy y mantenerse sano en el futuro.

NDEP National Diabetes Education Program
Un programa de los Institutos Nacionales de la Salud y los Centros para el Control y la Prevención de Enfermedades

Helping the Student with Diabetes Succeed

A Guide for School Personnel

Updated Edition 2010

U.S. Department of Health and Human Services
A Joint Program of the National Institutes of Health and the Centers for Disease Control and Prevention



National Diabetes Information Clearinghouse (NDIC) Resources

<http://diabetes.niddk.nih.gov/>

Continuous Glucose Monitoring

What is glucose monitoring?
Glucose monitoring helps people with diabetes manage the disease and avoid its serious problems. A person can use the results of glucose monitoring to make decisions about food, physical activity, and medications. The most common way to check glucose levels involves pricking a fingertip with an automatic lancing device to obtain a blood sample and then using a glucose meter to measure the blood sample's glucose level.

What is continuous glucose monitoring?
Continuous glucose monitoring (CGM) systems use a tiny sensor inserted under the skin to check glucose levels in tissue fluid. The sensor stays in place for several days to a week and then must be replaced. A transmitter sends information about glucose levels via radio waves from the sensor to a pager-like wireless receiver. The user must check blood samples with a glucose meter to program the device. Because currently approved CGM devices are not as accurate and reliable as standard blood glucose meters, users should confirm glucose levels with a meter before making a change to treatment.

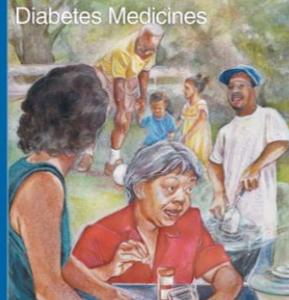


Alternative Devices for Taking Insulin

What alternative devices for taking insulin are available?
Insulin pens provide a convenient, easy-to-use way of injecting insulin and may be less painful than a standard needle and syringe. An insulin pen looks like a pen with a cartridge. Some of these devices use replaceable cartridges of insulin. Other pens are pre-filled with insulin and are totally disposable after the insulin is injected. Insulin pens never expire a date, but disposable needles on the tip of the pen expire on injection. There aren't any a date to check the amount of insulin. Inject the insulin, and press a plunger on the end to deliver the insulin just under the skin. Insulin pens are less widely used in the United States than in many other countries.



What I need to know about Diabetes Medicines



Your Guide to Diabetes: Type 1 and Type 2



Methods for Delivering Insulin and Monitoring Blood Sugar

A Review of the Research for Children, Teens, and Adults With Diabetes



Preventing Adverse Drug Events

Individualizing Glycemic Targets Using Health Literacy Strategies



Introduction ▼

Chapter 1 ▼

Chapter 2 ▲

Chapter 3 ▼

Chapter 4 ▼

Chapter 4 Overview

Shared Decision-Making
with Patients

**Applying Shared
Decision-Making**

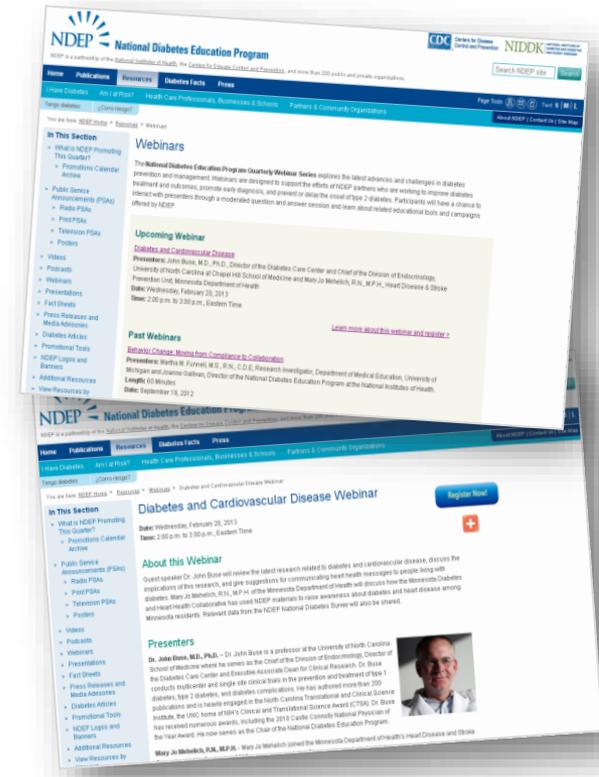
Key Points and
Knowledge Check

- *Preventing Adverse Drug Events:
Individualizing Glycemic Targets Using
Health Literacy Strategies*
- Earn continuing education credit (CME,
CNE, CEU, CPE)
- Available on the training tab of
www.health.gov



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 - www.YourDiabetesInfo.org/Webinars
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 - ndep@hagersharp.com



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