

Diabetes Treatment in a New Era: When to Begin Insulin and How to deliver it.



Objectives

1. Briefly review the evolution of insulin therapy.
2. Identify the types of insulin currently available for treatment of Type 2 DM.
3. Describe the action profiles of the different insulin therapies and relate these profiles to treatment regimens for patients with Type 2 DM.
4. Identify patients appropriate for insulin therapy in the treatment of Type 2 DM.
5. Recognize the barriers to the initiation of insulin therapy in patients with Type 2 DM and discuss strategies to overcome these barriers.
6. Review algorithms for the initiation of insulin therapy in patients with Type 2 DM.
7. Describe available insulin delivery systems.
8. Introduce new insulin therapies.

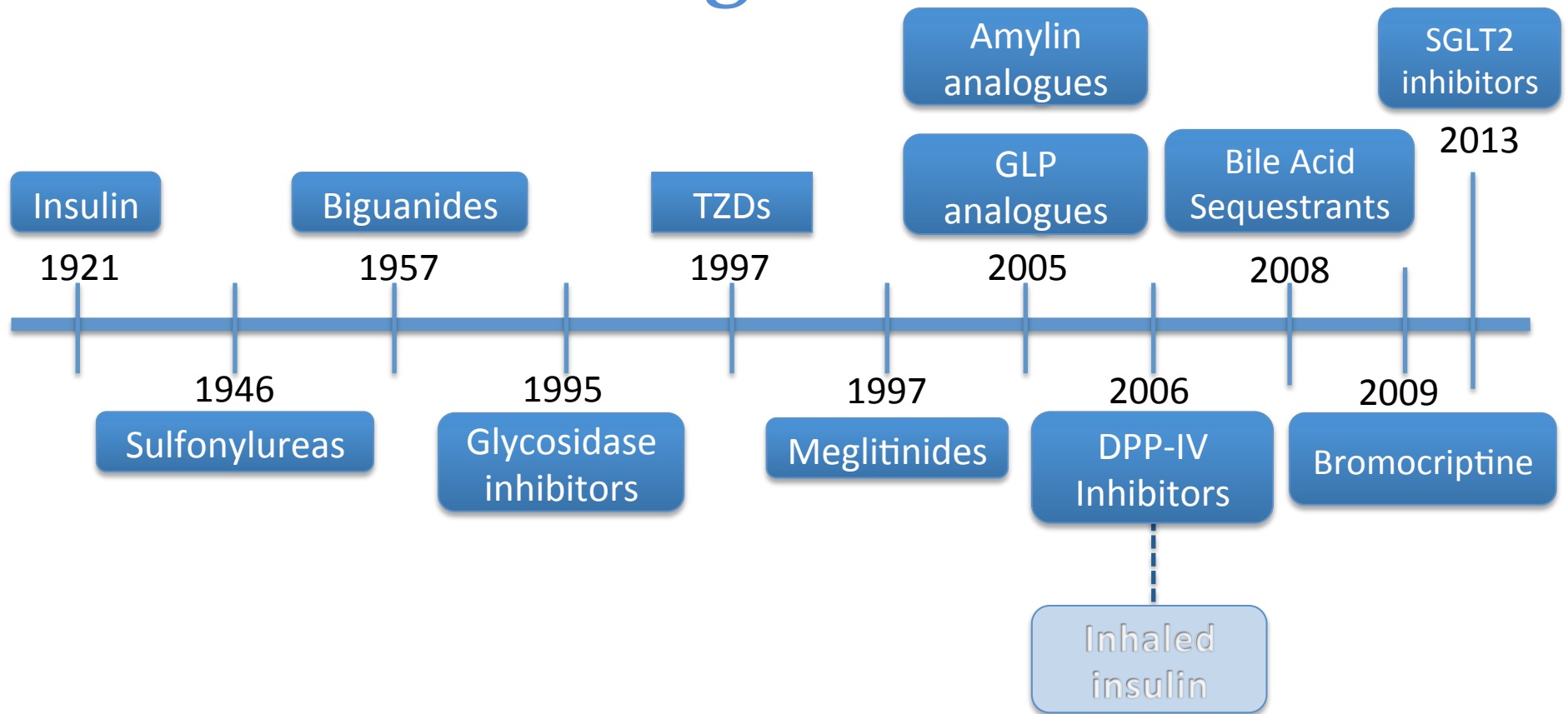
*Focus is Type 2 DM-adult nonpregnant patient



Questions to address:

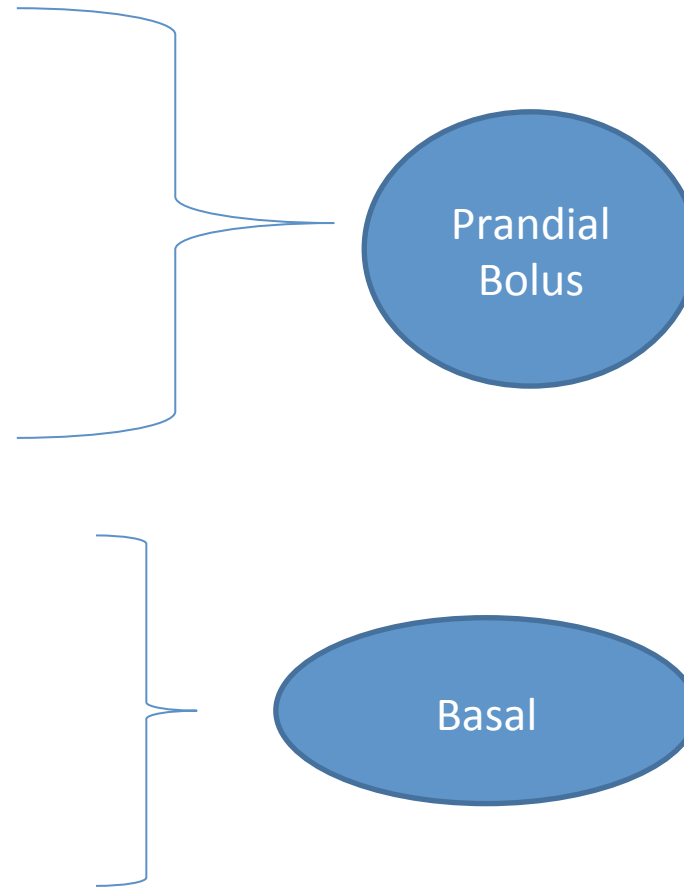
- What?
 - Insulin
- Why?
 - Evolution of insulin therapy to become more physiologic
- Who?
 - Appropriate patients for insulin therapy
- When?
 - Appropriate time to initiate insulin therapy and appropriate insulin regimen
- How?
 - Appropriate insulin delivery systems

Timeline of Antihyperglycemic Agents



Types of Insulin

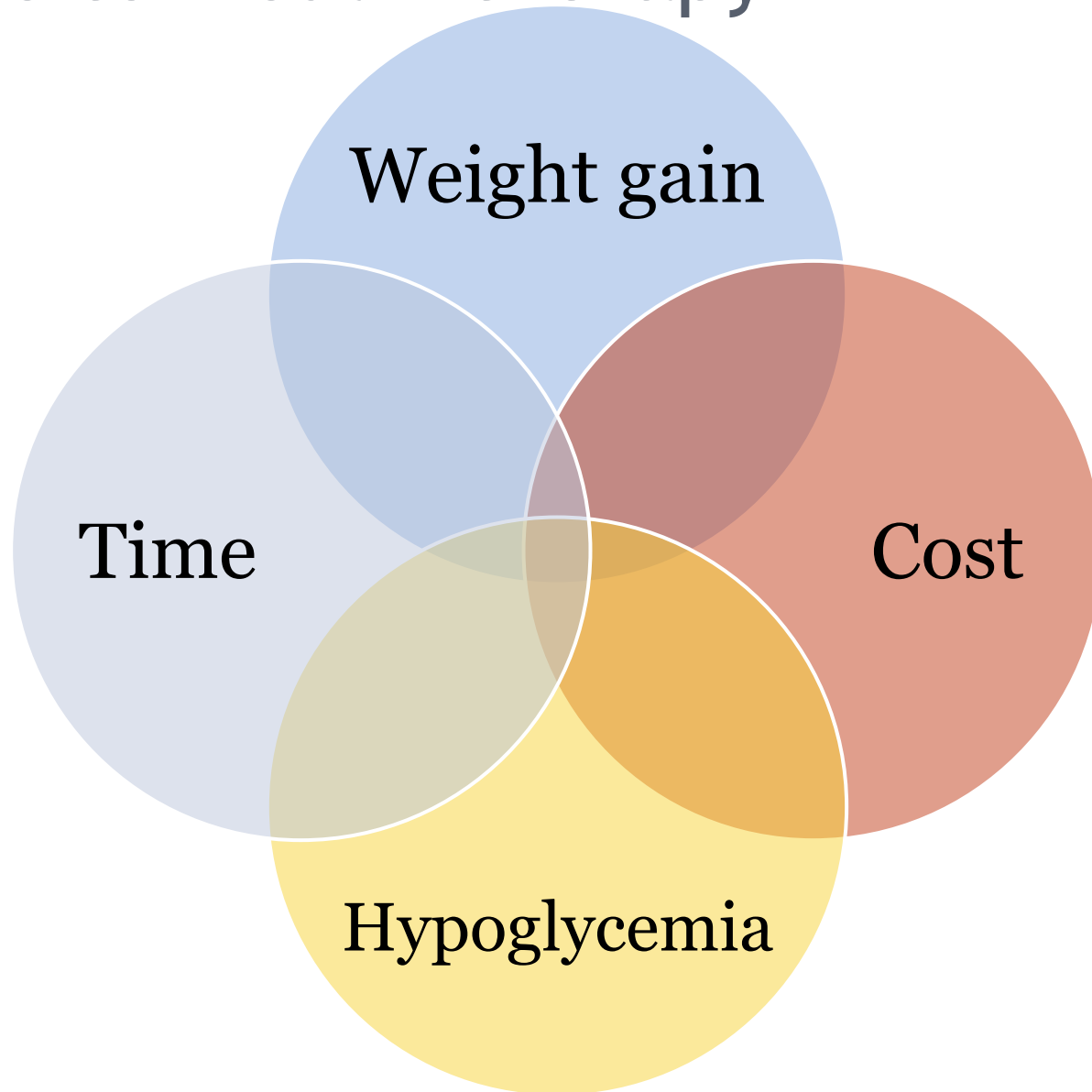
- **Rapid** acting (analogs)
 - Lispro (Humalog)
 - Aspart (Novolog)
 - Glulisine (Apidra)
- **Short** acting (human)
 - Regular (Humulin R, Novolin R)
- **Intermediate** acting (human)
 - NPH (Humulin NPH, Novolin NPH)
- **Long** acting (analogs)
 - Glargine (Lantus)
 - Detemir (Levemir)



INSULIN	FDA APPROVAL DATE
Rapid acting	
Lispro (Humalog)	June 1996
Aspart (Novolog)	November 2001
Glulisine (Apidra)	February 2004
Short acting	
Regular (Humulin R 100U)	October 1982
Regular (Novolin R)	June 1991
Intermediate acting	
NPH (Humulin N)	October 1982
NPH (Novolin N)	July 1991
Long acting	
Glargine (Lantus)	April 2000
Detemir (Levemir)	June 2005
Mix insulin	
70% NPH and 30% regular (Humulin 70/30)	April 1989
70% NPH and 30% regular (Novolin 70/30)	June 1991
50% insulin lispro protamine and 50% insulin lispro (Humalog 50/50)	June 1996
75% insulin lispro protamine and 25% insulin lispro (Humalog 75/25)	December 1999
70% insulin aspart protamine and 30% insulin aspart (Novolog 70/30)	November 2001

INSULIN	Onset (hrs)	Peak (hrs)	Duration (hrs)
Prandial/Bolus Insulin			
Rapid acting			
Lispro (Humalog)	0.1-0.25	0.5-3	4
Aspart (Novolog)	0.1-0.25	0.5-3	4
Glulisine (Apidra)	0.1-0.25	0.5-3	4
Short acting			
Regular	0.5-1	2-3	6-8
Basal			
Intermediate acting			
NPH	2-4	4-10	12-18
Long acting			
Glargine (Lantus)	2-4	Flat	20-24
Detemir (Levemir)	2-4	Flat	20-23

Barriers to insulin therapy





Barriers to Insulin Therapy

- Provider related
- Health system related
- Patient related

Barriers to Insulin Therapy

- Provider related
 - Physician beliefs
 - Pessimistic attitude toward disease
 - About the medication itself
 - ?efficacy
 - Weight gain
 - Hypoglycemia
 - Side effects
 - Physician concerns about patient dissatisfaction
 - Insulin therapy is inconvenient and painful for patients
 - Physician knowledge, treatment goals and experience
 - Time



Barriers to Insulin Therapy

- Health system related
 - Cost
 - Diabetes education

Barriers to Insulin Therapy

- Patient related
 - Fears
 - Weight gain
 - Needles/injections
 - Hypoglycemia
 - Diabetes complications
 - Failure
 - Impact on life/job
 - Cost and access
 - Comorbid depression

Barriers to Insulin Therapy

- Patient related:
 - Needle/injection
 - Is it a real barrier?
 - American Association of Diabetes Educators survey conducted by Harris Interactive examined a group of 500 patients who require insulin and showed that:
 - 33% of patients identified that they have some level of dread associated with taking their daily injections
 - 14% felt that the insulin injections had a negative impact on their life
 - 29% felt that injecting insulin was the hardest aspect of their diabetes care

BUT

- 52% did not proactively communicate with their healthcare team about quality of life issues

And these patients are already taking insulin

- Which is worse fear of the unknown or known?



Caution:

- Waiting too long to initiate insulin therapy
- Conversations about insulin as a threat or punishment
- Waiting too long to intensify regimen
- Not matching the regimen to the patient
- Clinical inertia
- Utilization of multiple noninsulin hyperglycemic agents at maximal doses without consideration of insulin therapy

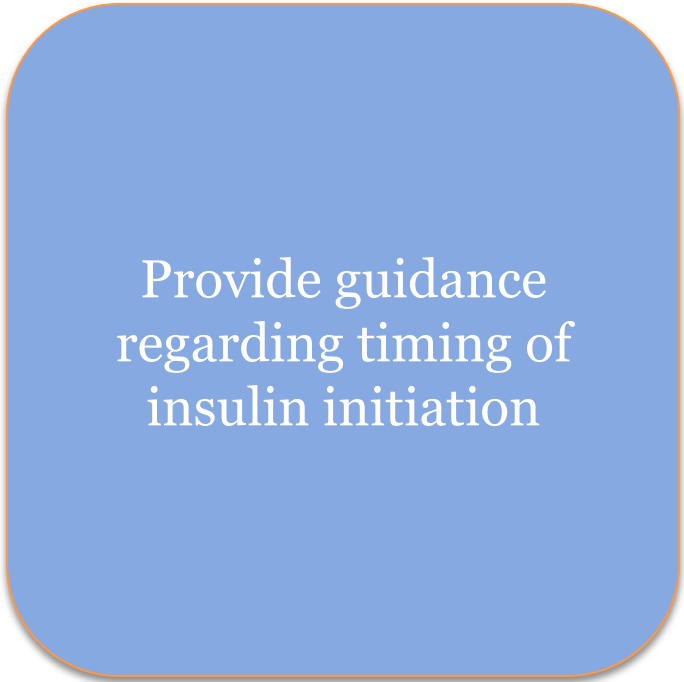


Goals of Insulin Therapy

- Achieve optimal glycemic control but avoid:
 - Hypoglycemia
 - Weight gain
 - Negative impact on patient's lifestyle
- Understand the appropriate glycemic target for the individual patient

Algorithms for management of Type 2 DM

- American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) Comprehensive Diabetes Management Algorithm
- Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)



Provide guidance regarding timing of insulin initiation



Definitions

- Basal/Background
- Bolus/Prandial
- MDI

Definitions

- Augmentation
- Replacement
- Carbohydrate ratio
- Correction factor (sensitivity factor)



How to add insulin therapy

- Weight based calculation
- Fixed starting dose with patient self titration



Starting insulin

- **Varying strategies**
 - What can the patient do?
 - How is your office equipped?
 - How many injections daily and with which type of insulin?



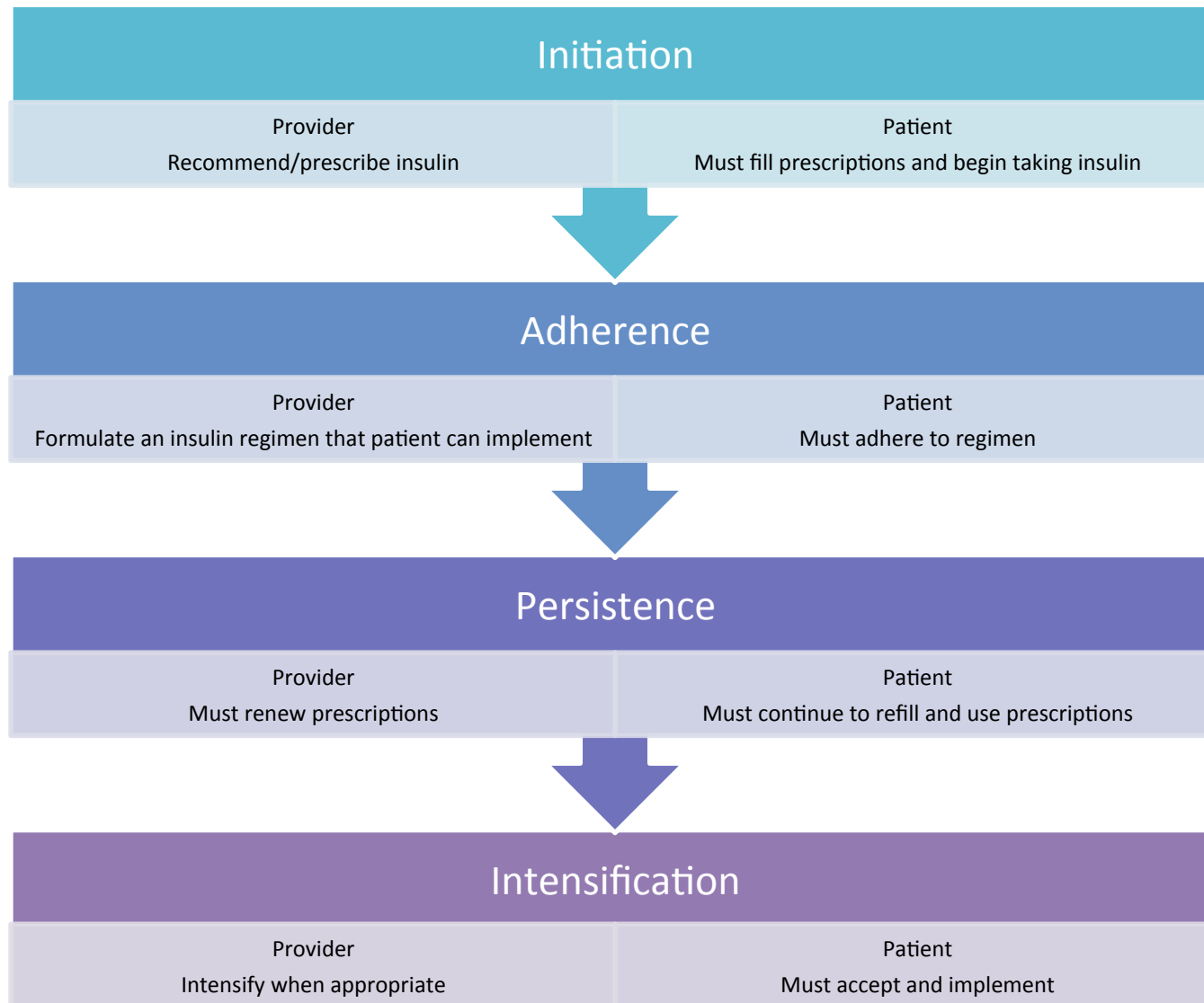
Algorithms for insulin initiation and titration

- American Association of Clinical Endocrinologists (AAACE) and American College of Endocrinology (ACE) Comprehensive Diabetes Management Algorithm
- Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) and update

Starting insulin

- Either weight based or fixed dose addition of basal insulin
- Caution with escalation of basal insulin without consideration of addition of prandial insulin
- Remember the physiology
- Consider addition of prandial insulin when basal insulin dose advanced to 0.5 units/kg

Effective insulin therapy



Peyrot, M., Barnett, A. H., Meneghini, L. F. and Schumm-Draeger, P.-M. (2012), Insulin adherence behaviors and barriers in the multinational Global Attitudes of Patients and Physicians in Insulin Therapy study. *Diabetic Medicine*, 29: 682–689.



Effective Insulin Regimen

- Tailor to the patient
 - Lifestyle needs
 - Physical and mental health and capabilities
 - Individual physiologic requirements
 - Weight
 - Insulin resistance
 - Comorbid conditions



Insulin Delivery


- Vial and syringe
- Insulin pens
- Insulin pumps

Challenges to insulin therapy

- Adherence to insulin therapy is lower than adherence to oral antihyperglycemic agents¹
- The challenges of therapy maintenance parallel barriers to initiation
 - Hypoglycemia
 - Weight gain
 - Regimen
- 1/3 of patients take insulin as prescribed²

¹Wallia, A., Molitch, M.E. (2014). Insulin Therapy for Type 2 Diabetes Mellitus. *JAMA*. 311(22):2315-2325.

²Peyrot, M., Barnett, A. H., Meneghini, L. F. and Schumm-Draeger, P.-M. (2012). Insulin adherence behaviors and barriers in the multinational Global Attitudes of Patients and Physicians in Insulin Therapy study. *Diabetic Medicine*, 29: 682–689

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- **6/27/2014 (updated 6/30/2014)**
 - **FDA approves Afrezza to treat diabetes**
 - The U.S. Food and Drug Administration today approved Afrezza (insulin human) Inhalation Powder, a rapid-acting inhaled insulin to improve glycemic control in adults with diabetes mellitus. Afrezza is a rapid-acting inhaled insulin that is administered at the beginning of each meal.

From the FDA

Afrezza

- **Ultra rapid acting mealtime insulin**
 - First in class
 - Peak insulin levels 12 to 15 minutes after inhalation
 - Cleared in 2-3 hours
- **Administration**
 - Dose (powder form contained in a cartridge)
 - Cartridge place in whistle sized inhaler

Afrezza

- Side effects (in clinical trials)
 - Hypoglycemia
 - Cough
 - Throat pain or irritation
- **Black box warning**
 - Acute bronchospasm
- Do NOT use:
 - Smokers
 - COPD
 - Asthma
 - DKA

- **2/25/2015**
 - **FDA approval of Toujeo (U-300 insulin glargine)**
 - 300 units per mL of insulin glargine

From the FDA

New Insulins in the Pipeline

- New generation basal insulin analogs
 - Degludec
 - What is it?
 - Insulin analog with a fatty acid side chain
 - Very long duration of action
 - Potential therapeutic advantages
 - Less fluctuation in glycemic control
 - Do not need to take at exact same time of day-greater flexibility of dosing
 - Less hypoglycemia
 - Concerns
 - Cardiovascular safety

NOT FDA APPROVED FOR USE

New Insulins in the Pipeline

- New generation basal insulin analogs
 - PEGylated Lispro
 - What is it?
 - Insulin Lispro + polyethylene glycol chain
 - Long half-life (2-3) days
 - Hepatopreferential effect (like endogenous insulin)
 - Potential therapeutic advantage
 - Less weight gain
 - Safety concerns?

NOT FDA APPROVED FOR USE



Don't Forget

- Conversation
 - Early
- Education

Additional References

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