Clinical Case Studies: Effective Strategies for Improving Insulin Initiation and Overcoming Barriers to Insulin Therapy

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Learning Objectives

- Review interprofessional approaches that maximize patient engagement in the diabetes care plan and achieve individual treatment goals.
- Apply best practices that the interprofessional team should employ when initiating insulin therapies.
- Apply effective strategies for managing patients who exhibit psychological insulin resistance.
- Explain strategies for improving adherence to insulin therapy.
- Review effective techniques for overcoming therapeutic inertia.

Initiating and Titrating Insulin Therapy: Engaging the Patient to Achieve Therapeutic Goals

Curtis L. Triplitt, Pharm.D., CDCES

Greg

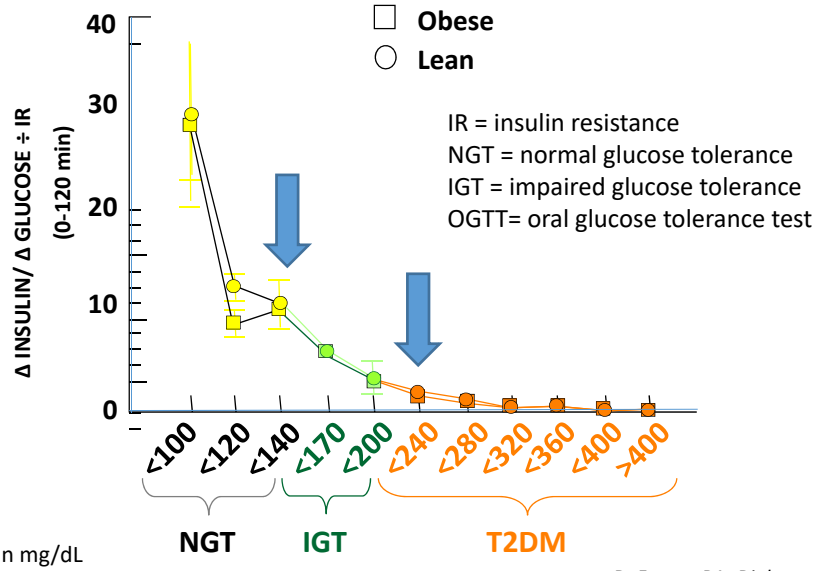
Age 67 y.o. Male with T2DM X16 years

- PMH
  - HTN
  - Dyslipidemia
  - Mild-NP DM Retinopathy
  - Obesity (100 kg)
- Current medications
  - Metformin 1 gram BID
  - Canagliflozin 300 mg daily
  - Lisinopril 40 mg PO daily
  - Atorvastatin 40 mg PO daily

- He follows a fairly healthy diet and takes his medications as prescribed
- Labs and BP are all normal except:
  - A1C 8.6% (3 days ago)
  - Was 8.2% 2 months ago

Long acting basal insulin daily 20 units at bedtime is started
Is this appropriate?

Progressive Beta-Cell Dysfunction in Prediabetes and T2DM*



* OGTT Glucose values in mg/dL

DeFronzo RA. *Diabetes*. 2009; 58:773-95.

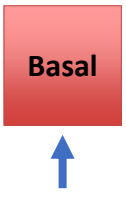
When is Insulin Appropriate?

- A1C>10% or blood glucose levels >300 mg/dL
- Any time glycemic control is inadequate on other therapies
- Type 1 DM is suspected
- Ongoing metabolic catabolism
  - Weight loss
  - Ketosis
  - Very high triglycerides
- Pregnancy

American Diabetes Association. *Diabetes Care*. 2020;43(suppl 1):S98-S110.

Type 2 DM: Building an Insulin Regimen

At Bedtime (NPH)
Or
Every 12-24 hours

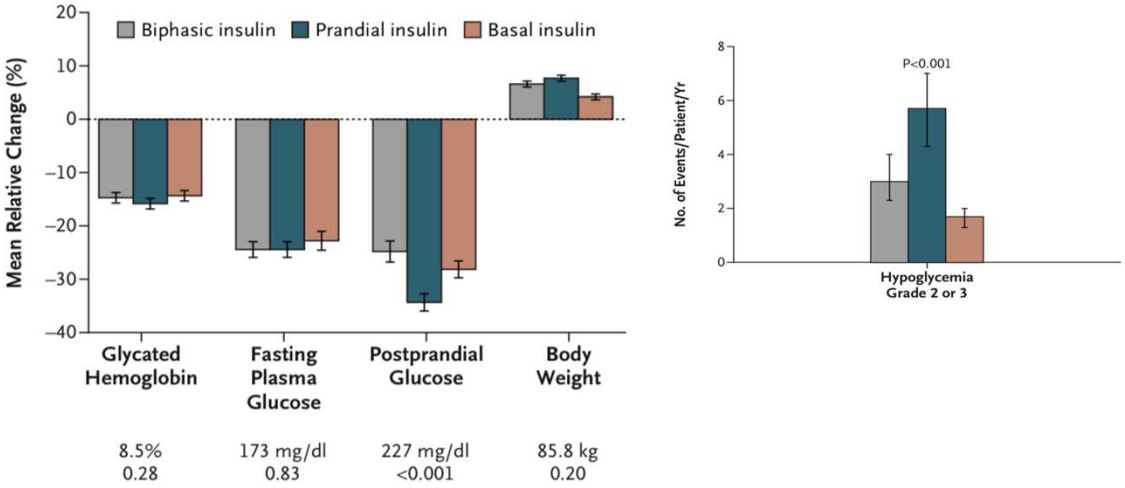


- Fewer injections/day
- Easier to start versus more complex insulin regimens
- Improves FPG and glycemic control in majority of patients
- Similar long-term glycemic control with less initial hypoglycemia versus more complex insulin regimens

Holman RR et al. *N Engl J Med* 2007; 361:1736-47. Adapted from: Moghissi ES et al. *Endocr Pract.* 2009;15(4):353-69.
Clement S et al. *Diabetes Care.* 2004;27(2):553-91.

Basal vs. Prandial vs. Premix Insulin

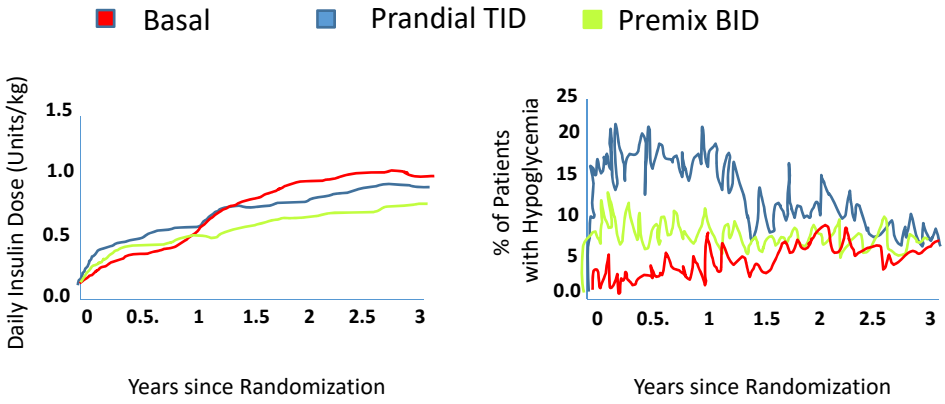
3-year Data



Holman RR. et al. *N Eng J Med.* 2009; 261:1736-47.

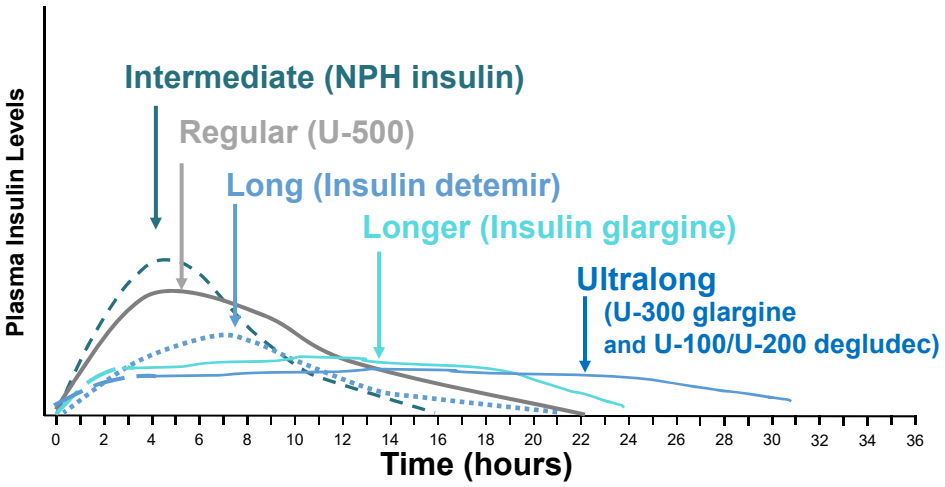
4T Trial: 3 Year Data

Insulin Dose and Hypoglycemia



Adapted from Holman RR et al. *N Eng J Med.* 2009; 261:1736-47.

Select Basal Insulin Choices



®

Adapted from Hirsh IB. *NEJM*. 2005;352:174-83. Flood TM. *J Fam Pract*. 2007;56(suppl 1):S1-12. Becker RH, et al. *Diabetes Care*. 2014;pii:DC_140006. http://www.pdr.net/full-prescribing-information/ for Afrezza and Fiasp. Accessed January 10, 2020

Basal Insulins Available*

Insulin	Time to Onset (hr)	Time to Peak Action (hr)	Duration of Action (hr)
Insulin human regular (U-500)	0.25	4-8	13-24
Intermediate-Acting Insulin			
Human insulin isophane (NPH)	2-4	4-10	12-18
Long-Acting Insulins			
Detemir	2-3	6-8	Up to 24
Glargine (U-100)	1-2	flat	20-24
Ultra-long Acting Insulins			
Glargine (U-300)	1-2	flat	up to 36
Degludec (U-100, U-200)	1	flat	>42
GLP-1RA Mix with Basal Insulin "Fixed Ratio Combinations"			
Lixisenatide and Glargine (U-100)	1-2	flat	20-24
Liraglutide and Degludec (U-100)	1	flat	>42

Patient-specific onset, peak, and duration may vary from times listed in table. *Pre-mix products not depicted

Hirsch IB. *N Engl J Med*. 2005; 352:174-83; Umpierrez GE et al. *J Clin Endocrinol Metab*. 2012; 97:16-38; Dansinger M. Types of insulin. June 21, 2016. www.webmd.com/diabetes/guide/diabetes-types-insulin (accessed 2020, January); Bennett JA. Insulin chart. July 17, 2015. Individual product package insert prescribing information.

Starting and Titration of Basal Insulin

Every 24 hour long-acting insulin OR bedtime intermediate-acting insulin

Daily dose: 10 units or 0.1-0.2 units/kg/day

Check FBG daily

Increase dose by 2-3 units every 2-3 days until FPG at desired goal

Check FBG daily

In the event of hypoglycemia or FPG level <70 mg/dL:

Reduce insulin dose by 4 units, or by 10-20%

OR

Check FBG daily

Treat to Target

FPG over last 2-3 days	Basal Insulin Adjustment
>180mg/dl	+8 units
140-180	+6 units
120-140	+4 units
100-120	+2 units
Below goal	-2 to -4 units

FPG = fasting plasma glucose

Philis-Tsimikas A. *Adv Ther*. 2013;30:607-22. American Diabetes Association. *Diabetes Care*. 2020;43(suppl 1):S98-110.

Are National Diabetes Organizations Recommendations in Line with This?

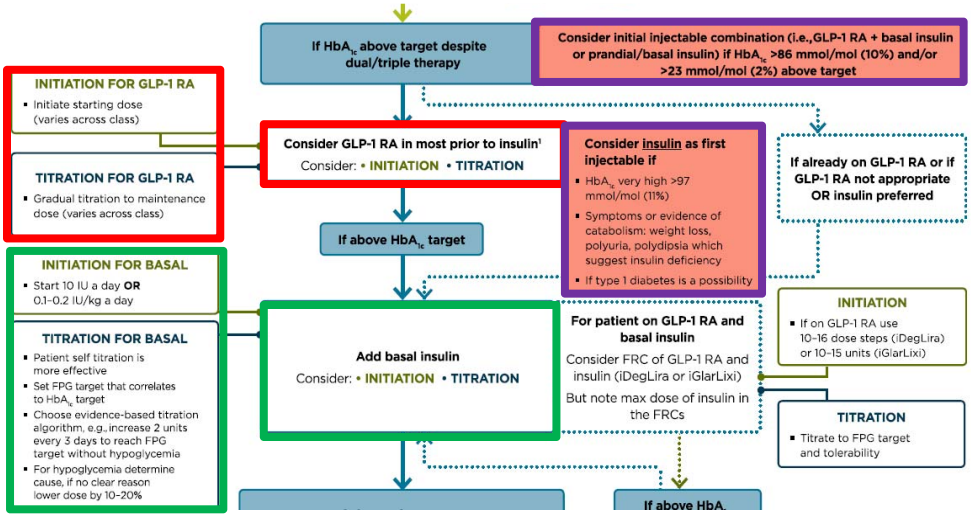
ADA: Pharmacologic Approaches to Glycemic Treatment

AACE/ACE. *Endocrine Practice* 2019;25(1):69-204.

American Diabetes Association. *Diabetes Care*. 2020;43(suppl 1):S98-110.

American Diabetes Association 2019* Injectable Therapy Recommendations

*Presented instead of 2020 as more detail given



Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes - 2019. *Diabetes Care.* 2019;42(Suppl 1):S90-102.

Greg

- Current medications
  - Metformin 1 gram BID
  - Canagliflozin 300 mg daily
  - Lisinopril 40 mg PO daily
  - Atorvastatin 40 mg PO daily
- Labs and BP are all normal except:
  - A1C 7.7% (1 day ago)
  - Was 8.1% 2 months ago
- Long-acting basal insulin 46 units at bedtime
- But 2X/week has awoken at 3AM "feeling funny"
- Self-monitored blood glucoses were 54 and 62 mg/dL
- Episodes were treated with orange juice

Long-acting basal insulin was discontinued:
Ultralong Acting Concentrated Insulin 40 units daily was started
Is this an appropriate change to address nocturnal hypoglycemia?

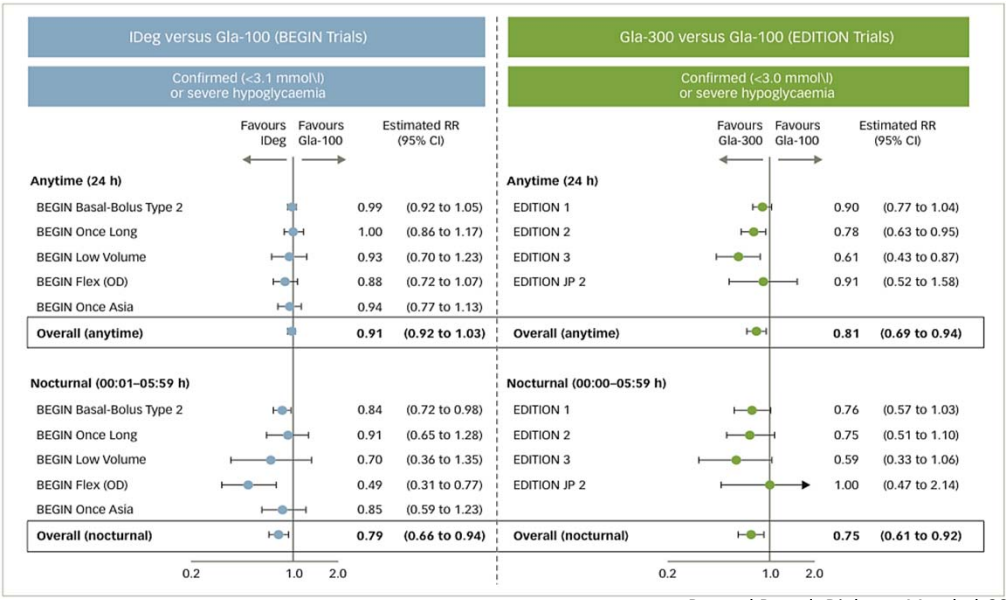
Conversion Between Basal Insulins

Conversion From:	To Other Basal Insulin	NOTES
NPH	NPH Daily = Unit-per-Unit NPH BID= Reduce dose 20%	
U-100 Glargine	Unit-per-Unit	
Detemir	Unit-per-Unit	Conversion to detemir- if <0.3 units/kg, administer BID May need slightly higher dose
U-300 Glargine	Unit-per-Unit	May need slightly higher dose
U-100 or U-200 Degludec	Units-per-Unit	
U-500 Regular	Conversion to U500 Regular (Split dose BID or TID) A1C≤8%= Lower Total Daily Dose of Insulin 20% A1C>8%= Convert Total Daily Dose unit-per-unit	

Basal Insulins: Efficacy is "Similar," but Hypoglycemia Risk Varies

Madenidou A-V et al. *Ann Int Med.* 2018;169:165-74.

Insulin Degludec and Insulin Glargine: Phase 3 Trials



Roussel R et al. *Diabetes Metabol*. 2018; 44:402-9.

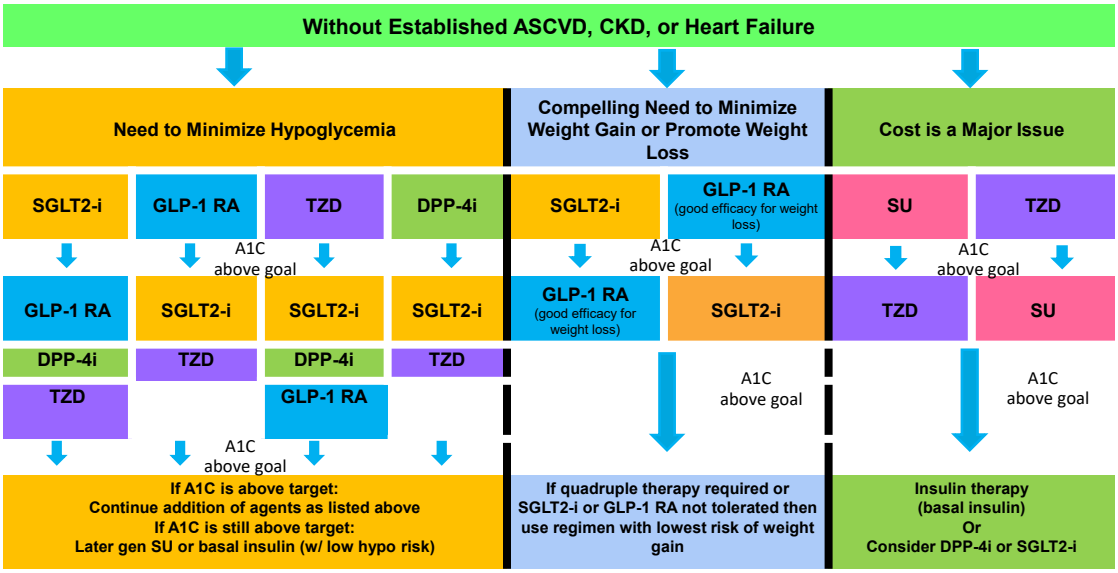
Insulin Degludec vs. Insulin Glargine (U300)

	Duration (weeks)	A1C (%) GLAR	A1C (%) DEG	ALL Hypo (95% CI)	Nocturnal Hypo (95% CI)	Severe Hypo (95% CI)
BRIGHT (Sanofi)	24	-1.64% *P*=NS	-1.59%	0.88 (0.66-1.17)	0.99 (0.74-1.32)	1 episode GLAR U300
CONCLUDE (Novo Nordisk, Inc.)	88	DEG -0.1% (-0.18 to -0.02) *P*=0.02		0.88 (0.73-1.06)	0.63 (0.48-0.84)	0.2 (0.7-0.57)
DEVOTE (Novo Nordisk, Inc.) U100 Glargine	2 years	0.01% (-0.05 to 0.07)			"Severe" 0.47 (0.31-0.73)	0.60 (0.48-0.76)

Hypo: hypoglycemia
Glar: insulin glargine
Deg: insulin degludec

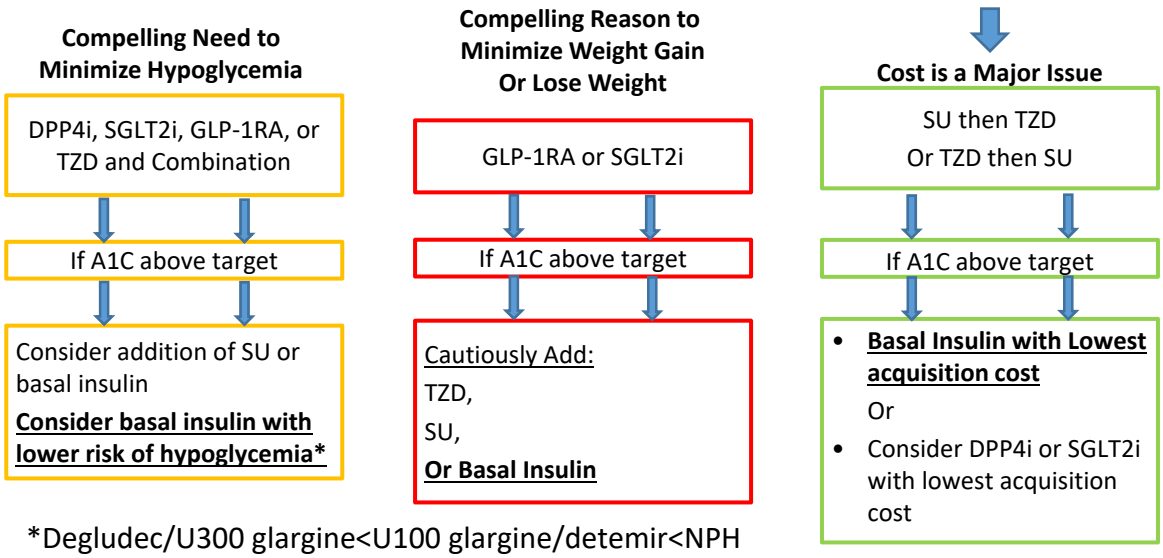
Rosenstock et al. *Diabetes Care.* 2018;41:2147-54.
Cheng A et al. *Diabet Obes Metab*. DOI: 10.1111/dom.13901.
Philis-Tsimikas A et al. *Diabetologia.* 2020;63:698-710.

ADA: Pharmacological Therapy Recommendations



Adapted from ADA Standards of Care. *Diabetes Care*. 2020; 43(Suppl 1):S1-S212.

Basal Insulin: ADA Pharmacologic Therapy Recommendations



*Degludec/U300 glargine<U100 glargine/detemir<NPH

Adapted from ADA Standards of Care. *Diabetes Care*. 2020; 43(Suppl 1):S1-S212.

Basal Insulin: ADA Pharmacologic Therapy Recommendations for:

ASCVD PREDOMINATES

- If further intensification is required or patient is now unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV safety:
  - For patients on a GLP-1 RA consider adding SGLT2i with proven CVD benefit
  - DPP-4i if not on GLP-1 RA
  - Basal insulin*
  - TZD
  - SU

HF or CKD PREDOMINATES

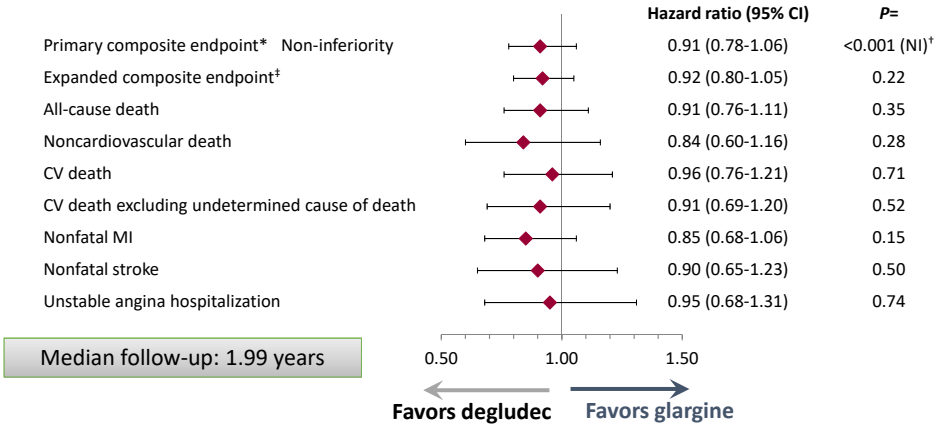
- Avoid TZD in the setting of HF. Choose agents demonstrating CV safety:
  - For patients on a SGLT2i, consider adding GLP-1 RA with proven CVD benefit
  - DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1RA)
  - Basal insulin*
  - SU

*Degludec or U100 Insulin Glargine have demonstrated CV safety

Adapted from ADA Standards of Care. *Diabetes Care*. 2020; 43(Suppl 1):S1-S212.

Cardiovascular Outcomes: Insulin Degludec vs. Glargine (U100)

DEVOTE CVOT Outcomes (*n*=7637)



*CV death, nonfatal MI, or nonfatal stroke; †Confirmed noninferiority; superiority, *P*=0.21.

‡CV death, nonfatal MI, nonfatal stroke, or hospitalization for unstable angina.

CI, confidence interval; CV, cardiovascular; MI, myocardial infarction; NI, noninferiority.

Marso SP et al. *N Engl J Med*. 2017;377:723-32.

Greg

- Current medications
  - Metformin 1 gram BID
  - Canagliflozin 300 mg daily
  - Lisinopril 40 mg PO daily
  - Atorvastatin 40 mg PO daily
- Labs and BP are all normal except:
  - A1C 7.5% (1 day ago)
- Has titrated to:
  - Ultra-long Acting Insulin 60 units (0.6units/kg) daily

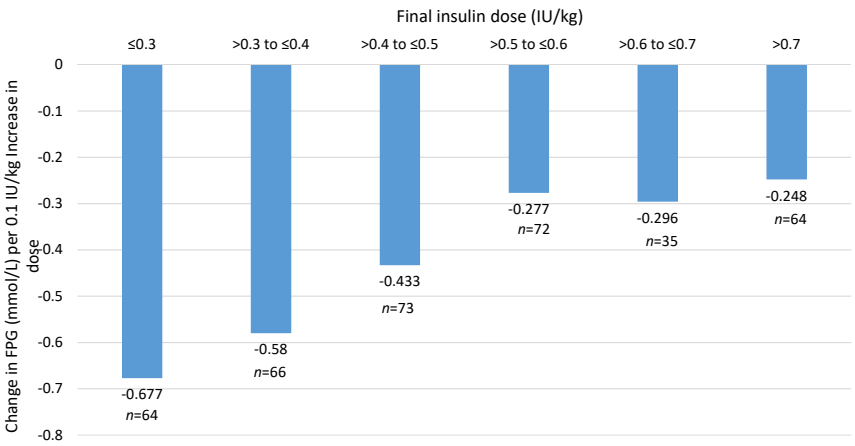
FPG and Bedtime Glucose (mg/dL) over last 7 days

FPG		172	72	92	130	70	182
Bedtime	232	164	162	142	172	222	

What would you recommend?
Titrate? Switch? Change regimen?

Basal Insulin and Overbasalization

Post-hoc analysis of 4, U-100 insulin glargine studies, ≥24weeks in duration

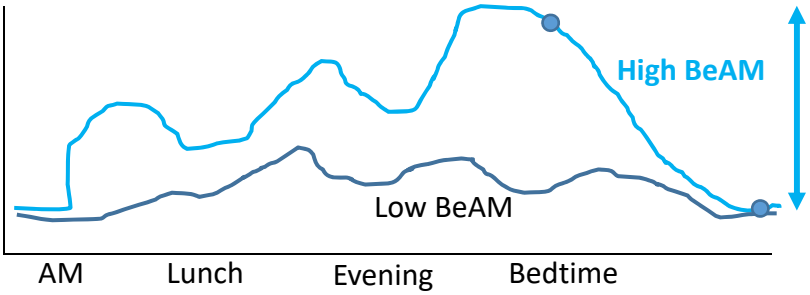


- Hypoglycemia did not significantly increase with higher dose
- Weight DID increase above 0.5units/kg

Umpierrez GE et al. *Diabetes Obes Metab.* 2019;1305-10.

Bedtime to Next Day Pre-Breakfast AM Glucose: (BeAM Value)

Easy Indicator to See if Intensification of Therapy May Be Appropriate



-BeAM >50mg/dL may indicate need to intensify therapy

Zinman A. *BMJ Open Diabetes Res Care.* 2016;4:e000171.

Fasting Plasma Glucose Variability (FPGV)

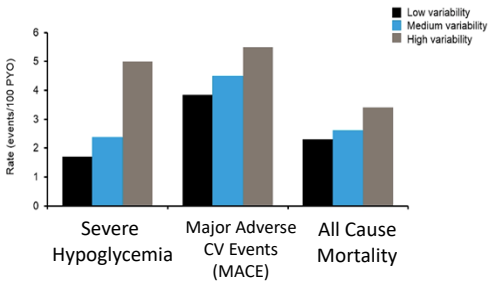
- FPGV may be associated with higher risk of complications
  - Higher risk of proliferative retinopathy and macular edema[1]
  - Associated with left ventricle wall thickness and LV ejection fraction[2]
  - FPGV associated with a 26% greater risk of CVD, and 46% higher risk of all-cause mortality in higher tertile[3]
- FPGV- limiting may negate risk
  - All-Cause Mortality no higher risk if mean/median variability <20%[4]

1. Hsieh YT et al. *Clin Exp Ophthalmol.* 2020; February 17 doi:10.1111/ceo.13728.
2. Tang X et al. *Cardiovasc Diabet.* 2019;18(50) https://doi.org/10.1186/s12933-019-0854-9.
3. Wang A et al. *JAHA.* 2017;6(12). https://doi.org.10.1161/JAHA.117.006757.
4. Zhao Q et al. *Diabetes Res Clin Pract.* 2019148:23-31.

Basal Insulin: Consequences of Fasting Plasma Glucose Variability (DEVOTE)

Fasting Glycemic Variability Associated Risks

Outcomes by variability tertile



Outcome	Hazard Ratio	95% CI	*P* value
Severe Hypoglycemia	3.37	2.52 to 4.5	<0.0001
3-Point MACE	1.21	0.98 to 1.49	0.08
All-Cause Mortality	1.33	1.01 to 1.75	0.04

Zinman B et al. *Diabetologia.* 2018;61:48-57.

Basal Insulin Goals and Greg

1. Control Fasting Plasma Glucose Levels
   - ✓Greg: Average FPG is 103 mg/dL
2. Avoid overbasalization
   - -Reassess benefit if >0.5 units/kg
     - -Greg: injects 0.6 units/kg of basal insulin
   - -Bedtime SMBG to AM SMBG is a high number
     - -Greg: Bedtime to AM glucose (BeAM) is 63 mg/dL
3. Consistent FPG readings (Low Fasting Glucose Glycemic Variability)
   - -Greg: FPG is 103 on average, but 5 out of 6 of FPG vary by >20%

1. Greg States: "I didn't think I would have to keep taking insulin"
2. Admits to omitting 2-3 injections per week
3. He feels hungry all the time, admits to overeating at times

SUMMARY: Basal Insulins

- Basal Insulin can help patients get to A1C goals
- Efficacy is similar between basal insulin options
- Be Patient Centered:
  - Understand the needs of your patient when starting and titrating basal insulin products
  - Ask about device options and cost
- Risk of hypoglycemia/nocturnal hypoglycemia may vary between basal insulin products
- Basal insulin has limitations:
  - Understand signs of need to intensify beyond basal insulin
  - Be cognizant of FPG variability- especially in CVD patients

Key Considerations in Initiating Insulin Therapy: Acknowledging and Overcoming Psychological Insulin Resistance

William H. Polonsky, Ph.D., CDCES
whp@behavioraldiabetes.org

Reluctance to Initiate IT

Reference	Type	Outcome
Polonsky, 2005	Survey (*n*=708)	28% "not willing"
Larkin, 2008	Survey (*n*=100)	33% "not willing
Cefalu, 2008	Multinational survey (*n*=975)	46% would avoid insulin
Polonsky, 2011	Multinational survey (*n*=1400)	17% "not willing"; 35% "ambivalent"

IT=insulin therapy

How Common is Initiation Delay?

- 3295 insulin-naïve T2Ds were identified who had been recommended insulin:
  - 984 (29.9%) declined
  - Of the 984 who declined, 374 (38%) eventually started insulin
  - Of the 374 who finally initiated, mean time to insulin initiation was 790 days

Hosomura N et al. *Diabetes Med.* 2017; 34:1599-602.

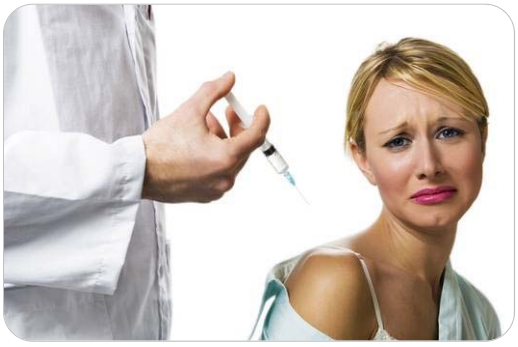
Obstacles to Insulin Initiation

Started IT?	Yes	No
Concerned about "side effects"	12%	44%
Concerned about hypoglycemia	16%	43%
Risks/benefits not explained	39%	55%
Not confident re-adjusting dose	12%	41%
IT self-care training provided	100%	16%

Karter AJ et al. *Diabetes Care.* 2010; 33:733-5.

Seven Initiation Obstacles

1. Injection-related anxiety
   - Discomfort with injections
   - Needle phobia



Seven Initiation Obstacles

2. Perceived lack of control
   - "If I start taking insulin, I'll never be able to stop."
   - "Taking insulin means no more spontaneity. It would restrict my life, making it too hard to travel, or eat out, or even have a life!"

Seven Initiation Obstacles

3. Low self-efficacy
   - "I'm just not confident I could handle the demands of insulin, like deciding how much to take and when to take it."
   - "It's just too complicated; it's too much for me to do."

Seven Initiation Obstacles

4. Personal failure
   - "If I take insulin, it means I have failed, that I haven't done a good enough job taking care of my T2D."

Peyrot M et al. *Diabetes Care.* 2005; 28:2673-90.

Seven Initiation Obstacles

5. Positive gain is not expected (DAWN)
   - 41% did not believe that IT might help to better glycemic control
   - 53% did not believe that IT might improve their health

Snoek FJ et al. *Health Qual Life Outcomes.* 2007; 5:69.

Seven Initiation Obstacles

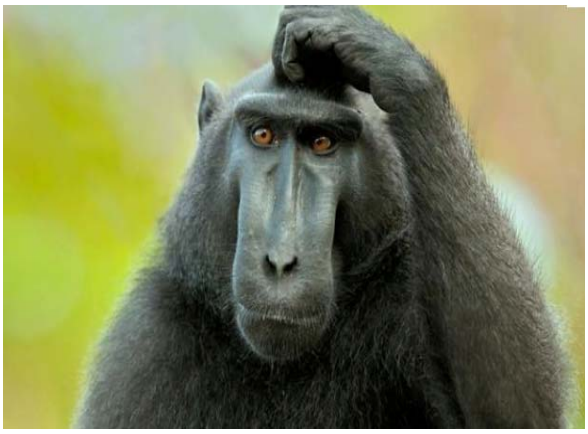
6. Concerns about adverse effects
   - Negative influence on work/social life
     - "My friendships may suffer (46%)."
   - Will lead to poorer health
     - IT "may cause hypo's, weight gain, or perhaps serious problems with my eyes or kidneys."
   - Represents sickness
     - "Starting insulin means I'm sicker, and my diabetes will become a more serious disease."

Yoshioka N et al. *Curr Med Res Opinion.* 2013; 30:177-83.

Seven Initiation Obstacles

1. Injection-related anxiety
2. Perceived lack of control
3. Low self-efficacy
4. A sense of personal failure
5. Positive gain is not expected
6. Concerns about adverse effects
7. **COST!**

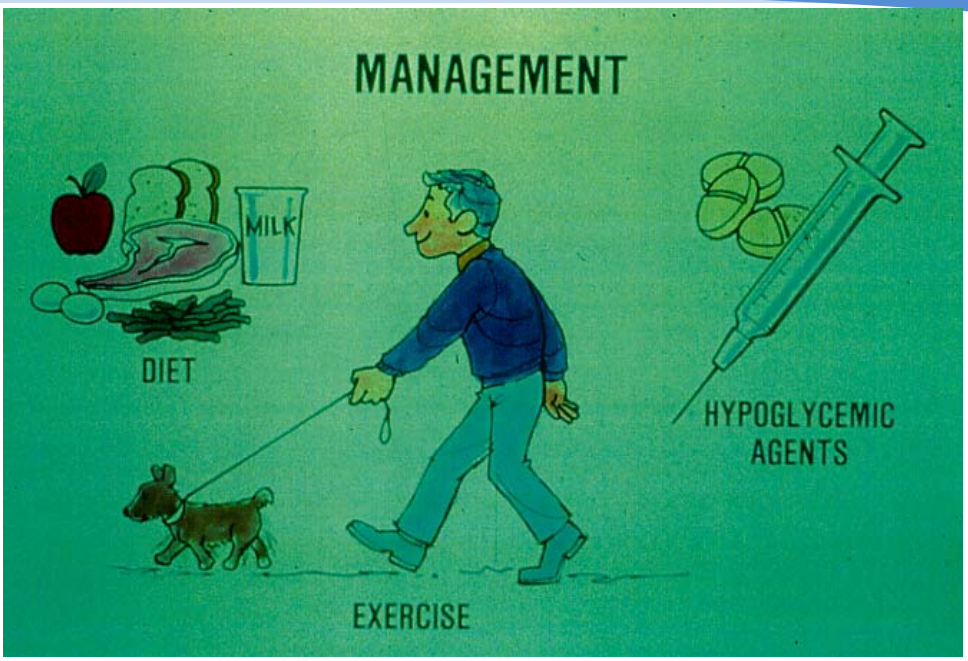
Why Such Negative Attitudes About Insulin?



Why Such Negative Attitudes?

- Observation of others with diabetes
  - "… all expressed deep-seated fears regarding side effects and the long-term health prognosis of insulin users, often citing poor health of family and friends who had used insulin." (*n* = 96)

Krall J et al. *Diabetes Technol Ther.* 2015; 17:268-74



Physician Influences

- Threatening patients with insulin
  - "If you can't make some positive changes in how you eat and exercise, then we'll have no choice but to start insulin."
- Underlying messages
  - Insulin should be avoided at all costs
  - You have failed
  - You are to be punished

"It's our job to help patients live as long as possible free of CVD complications. Although most patients share that goal, we don't always see the same pathways to get there.

I want to believe that if patients knew what I know, they would take their medicine. What I've learned is that if I felt what they feel, I'd understand why they don't."

Rosenbaum L. *NEJM* 2015;372:183-7.

Physician Resistance to Initiation

1. Lack of confidence
2. Presumption that patient will be unwilling and/or not compliant
3. Hypoglycemia and weight gain
4. No beneficial outcomes
5. Competing clinical demands

Haque M et al. *S Afr Med.* 2005; 95:798-802. Peyrot M et al. *Diabetes Care.* 2005; 28:2673-90.

So What To Do?

Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM

Identifying solutions to psychological insulin resistance: An international study☆

William H. Polonsky [a,b,*], Lawrence Fisher [c], Danielle Hessler [c], Heather Stuckey [d], Frank J. Snoek [e], Tricia Tang [f], Norbert Hermanns [g], Xavier Mundet [h], Maria Silva [i], Jackie Sturt [j], Kentaro Okazaki [k], Irene Hadjiyianni [l], Dachuang Cao [m], Jasmina Ivanova [n], Urvi Desai [n], Magaly Perez-Nieves [m]

- Retrospective survey, *n*= 594 T2Ds:
  - US, Germany, Canada, UK, Spain, Brazil, Japan
- All subjects indicated an initial unwillingness to start insulin, but had eventually done so.

Polonsky WH et al. *J Diabetes Complications.* 2019; 33:307-14.

Identifying Solutions to Psychological Insulin Resistance

- 38-item scale listed HCP statements/actions regarding IT initiation that may have occurred at medical visits.
- Each item rated on degree of helpfulness.
- EFAs then used to determine the key HCP action themes.

HCP=healthcare practitioner

Polonsky WH et al. *J Diabetes Complications.* 2019; 33:307-14.

Five Key HCP Action Themes

	Percent with ≥ 1 item occurring	Helpfulness (Mean (SD)
Demonstrated the Injection Process ("My HCP helped me to see that an injection wasn't as painful as I thought it might be")	94%	3.07 (0.74)
Explained Insulin Benefits ("My HCP told me that starting insulin could help me to live a longer and healthier life")	97%	2.97 (0.74)
Collaborative Style ("My HCP took time to answer all my questions and address my concerns about insulin")	95%	2.92 (0.78)
Dispelled Insulin Myths ("My HCP helped me to recognize that insulin was more natural than the pills I was taking")	89%	2.77 (0.72)
Authoritarian Style ("My HCP said that he/she could not continue to treat me if I refused to start insulin")	54%	2.63 (0.85)

Impact of HCP Action Themes

Table 4: Multivariate associations between perceived helpfulness of PAS Dimensions (pa behaviors

Perceived Helpfulness of HCP Actions	Delayed Start of Insulin	
	Odds Ratio (OR)	P-value
Demonstrated the Injection Process	0.75	0.01
Explained Insulin Benefits	0.77	0.12
Collaborative Style	0.88	0.44
Dispelled Insulin Myths	0.92	0.72
Authoritarian Style	0.92	0.47

Polonsky WH et al. *J Diabetes Complications.* 2019; 33:307-14

Impact of HCP Action Themes

Table 4: Multivariate associations between ı rticipant-reported HCP actions) and insuli behaviors

Perceived Helpfulness of HCP Actions	Discontinued Insulin Use (7+ Days)	
	Odds Ratio	P-value
Demonstrated the Injection Process	0.67	0.17
Explained Insulin Benefits	0.51	0.01
Collaborative Style	0.55	0.01
Dispelled Insulin Myths	0.67	0.07
Authoritarian Style	0.95	0.85

Polonsky WH et al. *J Diabetes Complications.* 2019; 33:307-14.

1. Encourage an Immediate Injection

- "Patients [*n* = 96]… found that giving an injection when insulin was introduced to be very helpful, yet in-office demonstration was reported by only one-half of the PCPs."

PCPs=primary care physicians

Krall J et al. *Diabetes Technol Ther.* 2015; 17:268-74.

2. Provide a Sense of Control

- The Insulin Challenge:

I'd like you to try insulin for just a month. At the end of the month, if you don't think its been worthwhile, or if it still seems as awful as you're imagining it might be, I promise to help you stop."

3. Ask/Address Personal Obstacles and Misbeliefs

"What are some of the reasons why taking insulin seems so bad to you?"

Addressing Insulin Misbeliefs

Obstacles	Discuss
It means I have failed	• No matter what you do, you may need IT, because diabetes is "progressive"
I will get complications	• Review those old family stories • Insulin is much more likely to reduce than raise complications risk
It means my diabetes is getting worse	• Insulin helps control BG levels and thus keeps the disease from getting worse
Insulin won't help	• List long-term benefits of good control • Nobel Prize not given for drugs that suck

Key Takeaways

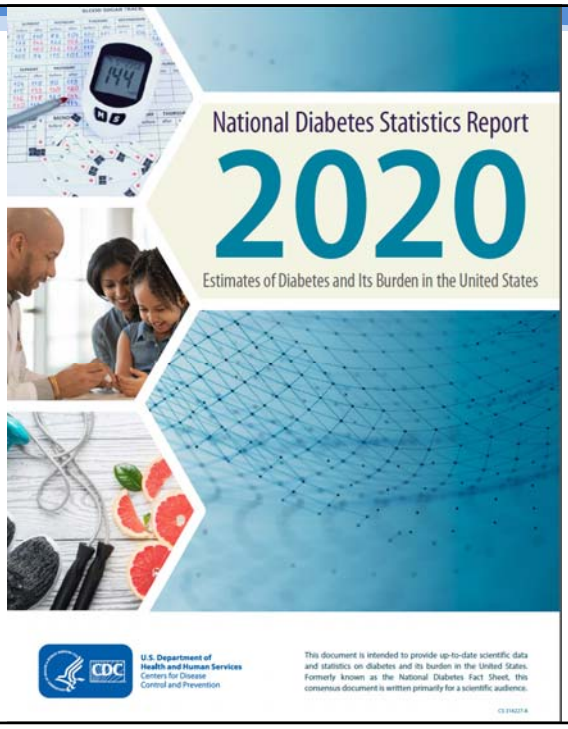
- Psychological Insulin Resistance is common
- Reluctant individuals have good reasons
- Four solutions:
  - Encourage an immediate injection
  - Provide a sense of control regarding IT
  - Ask/address personal obstacles and misbeliefs
  - And be collaborative!

Therapeutic Inertia in Diabetes Care: A Call for Action in Clinical Practice

Lawrence Blonde, M.D., FACP, MACE

Therapeutic Inertia in Diabetes Care: A Call for Action in Clinical Practice - Outline

- Prevalence of diabetes
- State of Diabetes Health Care Quality
- Clinical Inertia – Therapeutic Inertia
- Relationship of Hypoglycemia to Decreased Adherence in Insulin Treated Individuals with Diabetes
- Reduced hypoglycemia with longer acting basal insulin analogues
- Reduced hypoglycemia for those with T2D combining basal insulin analogues with GLP-1 receptor agonists vs. basal bolus insulin
- Need for timely intensification and deintensification of diabetes medications
- Some strategies to address Therapeutic Inertia

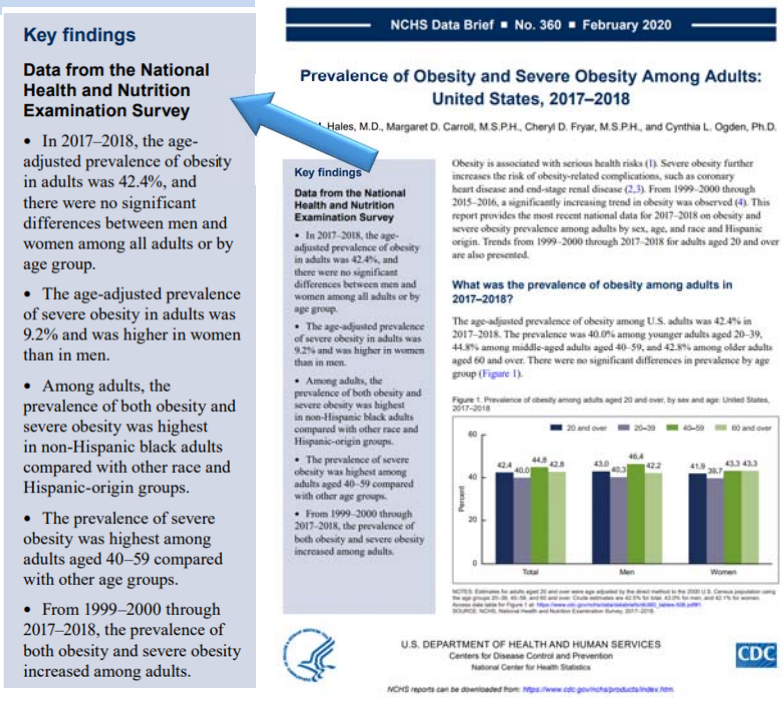


https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf

2018 Estimates of Prevalence of Diabetes Mellitus

- 34.2 million people of all ages (10.5% of the US population) had diabetes
- 34.1 million adults (13% of all US adults) had diabetes
- 7.3 million (21.4% of all US adults with diabetes) who met laboratory criteria for diabetes were not aware of or did not report having diabetes
- The percentage of adults with diabetes increased with age, reaching 26.8% among those aged 65 years or older

https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf



Key findings

Data from the National Health and Nutrition Examination Survey

- In 2017–2018, the age-adjusted prevalence of obesity in adults was 42.4%, and there were no significant differences between men and women among all adults or by age group.
- The age-adjusted prevalence of severe obesity in adults was 9.2% and was higher in women than in men.
- Among adults, the prevalence of both obesity and severe obesity was highest in non-Hispanic black adults compared with other race and Hispanic-origin groups.
- The prevalence of severe obesity was highest among adults aged 40–59 compared with other age groups.
- From 1999–2000 through 2017–2018, the prevalence of both obesity and severe obesity increased among adults.

NCHS Data Brief ■ No. 360 ■ February 2020

Prevalence of Obesity and Severe Obesity Among Adults: United States, 2017–2018

Hales, M.D., Margaret D. Carroll, M.S.P.H., Cheryl D. Fryar, M.S.P.H., and Cynthia L. Ogden, Ph.D.

Obesity is associated with serious health risks (1). Severe obesity further increases the risk of obesity-related complications, such as coronary heart disease and end-stage renal disease (2,3). From 1999–2000 through 2015–2016, a significantly increasing trend in obesity was observed (4). This report provides the most recent national data for 2017–2018 on obesity and severe obesity prevalence among adults by sex, age, and race and Hispanic origin. Trends from 1999–2000 through 2017–2018 for adults aged 20 and over are also presented.

What was the prevalence of obesity among adults in 2017–2018?

The age-adjusted prevalence of obesity among U.S. adults was 42.4% in 2017–2018. The prevalence was 40.0% among younger adults aged 20–39, 44.8% among middle-aged adults aged 40–59, and 42.8% among older adults aged 60 and over. There were no significant differences in prevalence by age group (Figure 1).

Figure 1. Prevalence of obesity among adults aged 20 and over, by sex and age: United States, 2017–2018

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Center for Health Statistics

NCHS reports can be downloaded from: https://www.cdc.gov/nchs/products/index.htm

https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf

Risk Factors for Diabetes-Related Complications

Among US adults aged 18 years or older with diagnosed diabetes, crude estimates for 2013–2016 shown in Appendix Table 8 were:

Smoking

- 21.6% were tobacco users based on self-report or levels of serum cotinine.
- 15.0% reported current cigarette smoking.
- 36.4% had quit smoking but had a history of smoking at least 100 cigarettes in their lifetime.

Overweight and Obesity

- 89.0% were overweight or had obesity, defined as a body mass index (BMI) of 25 kg/m² or higher. Specifically:
  - 27.6% were overweight (BMI of 25.0 to 29.9 kg/m²).
  - 45.8% had obesity (BMI of 30.0 to 39.9 kg/m²).
  - 15.5% had extreme obesity (BMI of 40.0 kg/m² or higher).

Physical Inactivity

- 38.0% were physically inactive, defined as getting less than 10 minutes a week of moderate or vigorous activity in each physical activity category of work, leisure time, and transportation.

A1C

- 50.0% had an A1C value of 7.0% or higher. Specifically:
  - 22.3% had an A1C value of 7.0% to 7.9%.
  - 13.2% had an A1C value of 8.0% to 9.0%.
  - 14.6% had an A1C value higher than 9.0%.
- 16.3% of adults aged 18–44 years had A1C levels of 10% or higher, compared to 12.7% of those aged 45–64 years and 4.3% of those aged 65 years or older (Appendix Table 9).

High Blood Pressure

- 68.4% had a systolic blood pressure of 140 mmHg or higher or diastolic blood pressure of 90 mmHg or higher or were on prescription medication for their high blood pressure (Appendix Table 8).

High Cholesterol*

- 43.5% had a non-HDL level of 130 mg/dL or higher. Specifically:
  - 22.4% had a non-HDL level of 130 to 159 mg/dL.
  - 11.2% had a non-HDL level of 160 to 189 mg/dL.
  - 9.9% had a non-HDL level of 190 mg/dL or higher.

https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf

Achievement of Target A1C <7.0% by U.S. T2D Pts Treated With Basal Insulin in Both RCTs and Clinical Practice

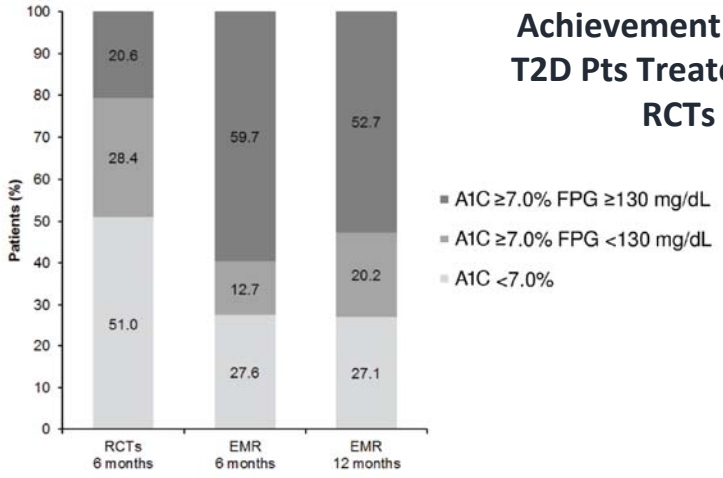


FIGURE 1. Proportion of patients stratified by achieved A1C and FPG targets at 6 and 12 months. The graph represents data from pooled RCTs from 11 24-week studies of patients initiating basal insulin between 2000 and 2005 and from outpatient EMR data from the GE Centricity database for insulin-naive patients initiating basal insulin between 2005 and 2012.

Blonde L et al. *Diabetes Spectrum.* 2019; 32(2): 93-103.

FROM RESEARCH TO PRACTICE

Overview of Therapeutic Inertia in Diabetes: Prevalence, Causes, and Consequences

Susan L. Karam, Jared Dendy, Shruti Polu, and Lawrence Blonde

Frank Riddick Diabetes Institute, Department of Endocrinology, Ochsner Medical Center, New Orleans, LA

Many people with diabetes do not achieve individualized treatment targets. Therapeutic inertia, the underuse of effective therapies in preventing serious clinical end points, is a frequent, important contributor to this failure. Clinicians, patients, health systems, payors, and producers of medications, devices, and other products for those with diabetes all play a role in the development of therapeutic inertia and can all help to reduce it.

The prevalence of total diabetes in the United States was 14% from 2013 to 2016, with a 9.7% prevalence of diagnosed diabetes and a 4.3% prevalence of undiagnosed diabetes (1). An estimated 1.5 million new cases are diagnosed every year (2). In 2017, the total estimated cost of diabetes was $327 billion; adjusted for inflation, this represents a 26% increase from 2012 to 2017 (3).

Type 2 diabetes, which accounts for 90–95% of all diabetes, is a progressive disease characterized by insulin resistance in most patients and impaired and declining β-cell function in virtually all (4). As a result, most patients require progressive intensification in therapy to reach and maintain glycemic goals. It is well established that meeting glycemic targets reduces the risk of development and progression of microvascular and probably macrovascular complications (5). Edelman and Polonsky (6) noted that, despite multiple importance to understand the barriers to achieving glucose targets.

One such barrier is therapeutic inertia, which can be driven by the physician, the patient, or both. In addition, the health care system, payers, and producers of antihyperglycemic therapies and diabetes medical devices can all potentially play a role. The aim of this review is to provide an overview of therapeutic inertia in patients with diabetes, including its prevalence, causes, and consequences or outcomes.

The term "clinical inertia" has been used since the early years of this century. Allen et al. (9) proposed that clinical inertia includes three factors: physician factors, patient factors, and office system factors. Clinical inertia denotes underuse of effective therapies in preventing serious clinical end points despite abundant evidence showing the

Karam SL et al. *Diabetes Spectrum.* 2020;33(1): 8-15.

Therapeutic vs. Clinical Inertia

- Proposed that the term "therapeutic inertia" is more appropriate to describe failure to advance or deintensify treatment, whereas broader concept of clinical inertia includes not only escalation or deintensification of therapy but also issues such as failure to screen, make appropriate referrals, and manage risk factors and complications.

Khunti K et al. *Primary Care Diabetes.* 2017;11(2):105-6.

Why does clinical inertia occur?

- **Clinician-level barriers**[1]
  - Inertia related to clinicians including time constraints, suboptimal knowledge/training, concern re potential risks of hypoglycemia/weight gain etc., variations in guideline recommendations and overestimating adherence to guidelines
- **Patient-level barriers**[1]
  - Inadequate adherence related to concerns including hypoglycemia, weight gain, other side effects and costs
- **Discontinuity of care**[2]
  - Failure of continuity of care i.e. the process by which the patient and their physician-led care team are cooperatively involved in ongoing health care management toward the shared goal of high quality, cost-effective medical care
- **System-level barriers**[1]
  - Due to issues in healthcare, including costs of care

1. Khunti S et al. *Br J Diabetes Vasc Dis.* 2015;15:65-9.
2. http://www.aafp.org/about/policies/all/definition-care.html (last accessed: 09 Apr 2020).

American Diabetes Association.

Overcoming Therapeutic Inertia

The American Diabetes Association is embarking on a new campaign, Overcoming Therapeutic Inertia: Accelerating Diabetes Care for Life, to address all the forces and factors that contribute to delay in implementing the most effective care for each person with diabetes. Here's the current diabetes landscape:

- In the last 20 years despite more technology, more education and more drug therapies the average A1C for a person with diabetes has not changed. The number of patients with an A1C over 9% has actually increased.
- Treatment intensification is significantly behind recommendations in the ADA Standards of Care.
- Only 5% of recently diagnosed patients with diabetes on Medicare are using Diabetes Self Management Education and Support.
- Based on recent studies, there is a significant gap in what patients say they are willing to do to reduce A1C and what physicians believe patients are willing to do to reduce A1C.
- Real time patient data indicates that within one year of a diabetes diagnosis, less than 50% of patients are still taking the prescribed medication.
- In 2017 $327 billion was spent on treatment of people with diagnosed diabetes ($237 direct medical costs and $90 million reduced productivity)

If additional drug therapies, more information, and better education and a wealth of new technologies are not the answer, then what is?

ADA's Overcoming Therapeutic Inertia initiative is supported by Founding Sponsors Abbott, AstraZeneca, Merck, Novo Nordisk and Sanofi, plus Strategic Sponsors Dexcom, Janssen, Lilly and Medtronic.

https://professional.diabetes.org/meeting/other/overcoming-therapeutic-inertia

Systematic Review of Therapeutic Inertia in Patients with Type 2 Diabetes

- 53 papers from January 2004 to August 2016
- In most, median time to treatment intensification after above target HbA1c was more than 1 year
- Therapeutic inertia increased as number of antihyperglycemic drugs rose and decreased with increasing HbA1c
- Authors concluded that therapeutic inertia in management of hyperglycemia in people with type 2 diabetes is major concern

Khunti K et al. *Diabetes Obes Metab.* 2018; 20(2):427-37.

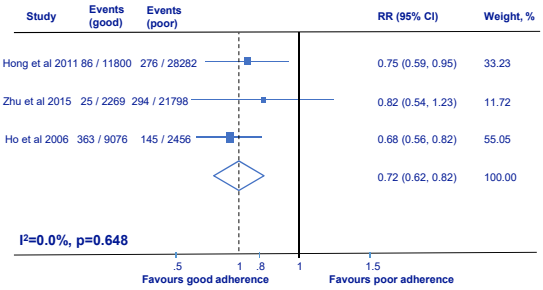
Gap Between Efficacy in RCTs and Effectiveness in Real-World Use of GLP-1 RA and DPP-4 Therapies

- Retrospective claims (Optum/Humedica) analysis to compare change in A1C of Real-World (RW) T2D pts 12 months after starting GLP-1 RA or DPP-4 inhibitor with published findings from RCTs.
- Selected RW pts were similar to RCT pts, and regression analysis was used in RW data to adjust for differences between poorly adherent and adherent patients to explain why RCT and RW findings may differ.
- Poor medication adherence accounted for ~ 3/4 of gap between RW and expected RCT results (gap = 0.51% [6 mmol/mol] GLP-1 RA; 0.18% [3 mmol/mol] DPP-4).

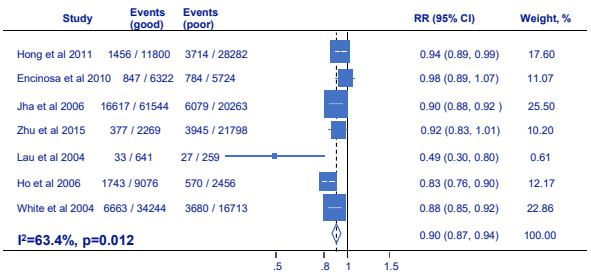
Carls GS et al. *Diabetes Care.* 2017;40(11): 1469-1478.

Poor Adherence Associated with Increased Hospitalization & Mortality

- Systematic review of 8 observational studies (318,125 patients with T2DM)
- Poor adherence was 37.8% (95% CI 37.6, 38.0)
- Good adherence associated with reduced:



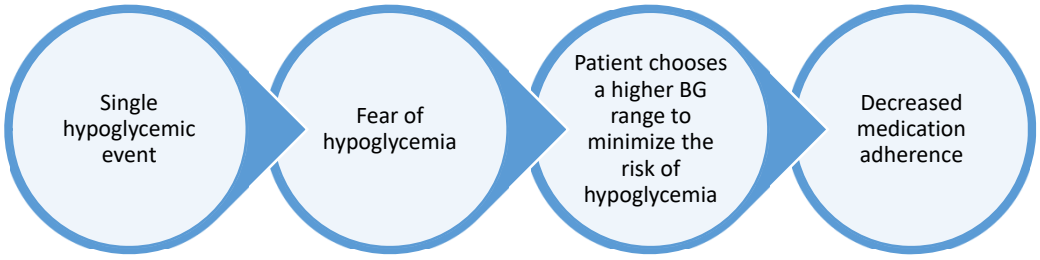
All-cause mortality 0.72 (95% CI 0.62–0.82)



All-cause hospitalization 0.90 (95% CI 0.87–0.94)

Khunti K et al. *Diabetes Care.* 2017;40:1588-96.

Hypoglycemia and Insulin Adherence



Hajós TR. *Diabetes Care*. 2014;37(1):102-8; Gonder-Frederick LA. *Diabet Med*. 2013;30(5):603-9.

Early Hypoglycemia & Adherence After Basal Insulin Initiation in Nationally Representative Sample of Medicare Beneficiaries With T2D

- Retrospective analysis of 5% sample of Medicare files identifying beneficiaries with T2D initiating BI from 1 January 2008 to 31 December 2012.
- Early hypoglycemia defined as ≥1 hypoglycemic event ≤6 months postindex. Outcomes included medication adherence and persistence over 12- and 36-month follow-up
- Of 14,466 patients, 1315 (9.1%) experienced hypoglycemia ≤6 months after initiating BI.
- At 12 months, patients with early hypoglycemia were less likely to be adherent to (OR 0.81 [95% CI 0.70–0.93]) and more likely to discontinue (OR 1.33 [95% CI 1.07–1.66]) their insulin therapy. Results similar at 36 months.

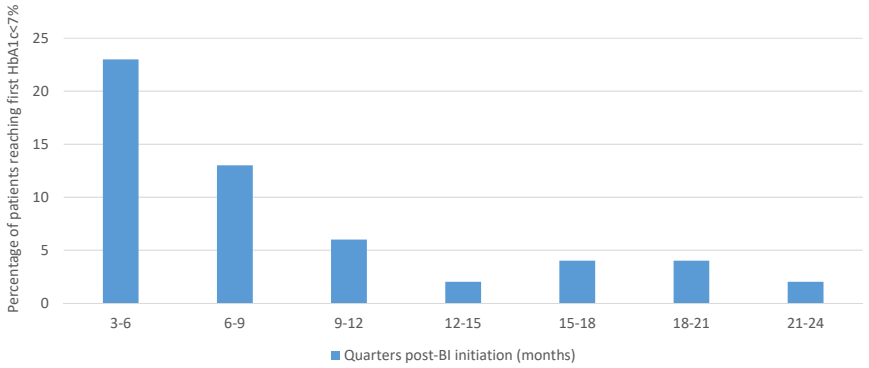
Li P et al. *Diabetes Obesity Metabolism.* 2019;21(11): 2486-95.

Benefits of Ultra-Long-Acting Basal Insulins Insulin Degludec and Insulin Glargine U-300

- Longer duration, Consistent once-daily dosing
- Less glycemic variability = Less hypoglycemia, especially nocturnal[1,2,3,4]
- May provide less weight gain[4,5]
- May lead to improved adherence[3]

1. Pettus J et al. *Diabetes Metab Res Rev*. 2016;32(6):478-96. 2. Yki-Jarvinen H et al. *Diabetes Obesity Metabolism*. 2015;17:1142-1149. 3. Mathieu C et al. *J Clin Endocrinol Metab*. 2013; 98(3):1154–62. 4. Yki-Jarvinen H et al. *Diabetes Care*. 2014;37:3235-43. 5. Melzer Cohen C et al. *Diabetes Ther*. 2017;8(5)1047-1005.

Conditional Probability of Goal Attainment



- Real-world data from large IBM Watson Health™ Explorys database suggested that among T2D patients initiating BI after OADs, likelihood of reaching glycemic control diminished over time, and remained low from 12 months onwards.
- Additional treatment options should be considered if patients do not reach glycemic control within 12 months of BI initiation.

Blonde L et al. *Diabetes Ther.* 2018; 9(3): 1169-84.

Post-insulin Intensification Inertia

- Retrospective cohort study of T2D in UK Clinical Practice Research Datalink database between January 2004 and December 2011, with follow-up until December 2013.
- Of 11,696 patients, 36.5% had treatment intensified during study period; 50.0, 42.5 and 7.4% intensified with bolus or premix insulin or GLP1-RA, respectively.
  - Median time from initiation of BI to intensification was 4.3 years [95% (CI) 4.1, 4.6].
- Among those with A1C ≥7.5%, 30.9% had regimen intensified.
  - Median time to intensification was 3.7 years (95% CI 3.4, 4.0).
  - 32.1% stopped basal insulin therapy.

Khunti K et al. Diabetes Obes Metab. 2016;18:401–9.

Antihyperglycemic Management in Older Adults at Hospital Discharge

- Retrospective cohort study of diabetes individuals ≥65 years not previously requiring insulin hospitalized in a Veterans Health Administration hospital for common medical conditions between 2012 and 2013
- 1 in 10 hospitalized older adults with diabetes was discharged with intensifications to their outpatient antihyperglycemic regimens
- Most intensifications were new initiations of insulins and sulfonylureas in response to increased inpatient BG levels
- 49% had limited life expectancy or had already achieved an outpatient A1C < 7.5% & not likely to benefit
- Only 20% of those with potential to benefit from stricter glycemic control, received intensifications
- Authors stated need to move toward more patient-centered decision-making considering long-term benefits and risks

Anderson TS et al. JAMA Network Open. 2020;3(3): e201511-e201511.

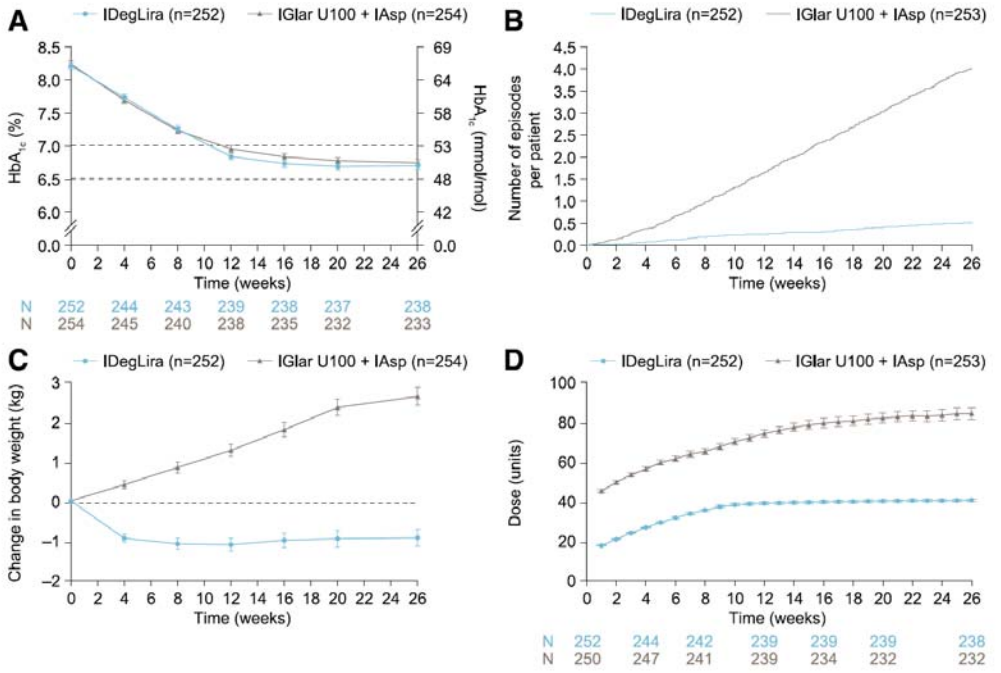
Diabetes Care Volume 41, May 2018 1009

Efficacy and Safety of IDegLira Versus Basal-Bolus Insulin Therapy in Patients With Type 2 Diabetes Uncontrolled on Metformin and Basal Insulin: The DUAL VII Randomized Clinical Trial

Liana K. Billings,[1,2] Ankur Doshi,[3] Didier Gouet,[4] Alejandra Oviedo,[5] Helena W. Rodbard,[6] Nikolaos Tentolouris,[7] Randi Grøn,[8] Natalie Halladin,[8] and Esteban Jodar[9]

Diabetes Care 2018;41:1009–1016 | https://doi.org/10.2337/dc17-1114

Billings LK et al. *Diabetes Care*. 2018;41(5): 1009-1016.



Billings LK et al. *Diabetes Care*.2018;41(5): 1009-1016.

Continuous Glucose Monitoring vs. Usual Care in Participants with T2D Receiving Multiple Daily Insulin Injections

Background	Continuous glucose monitoring (CGM) beneficial for adults with T1D but not well-evaluated in insulin treated T2D individuals
Patients/ Intervention	158 adults; T2D for a median of 17 years. Random assignment to CGM or usual care for 24 weeks
Results	Mean HbA1c levels decreased from 8.5% to 7.7% in CGM group vs. 8.0% in controls

Beck RW et al. *Ann Intern Med.*2017;167(6): 365-374.

Effects of Smart Connected Insulin Pen

- Observational study of effect of connected insulin pen on insulin regimen adherence and glycemic control
- 94 individuals with T1D on BBI regimen and CGM from 12 Swedish diabetes clinics downloaded pen data at each visit
- TIR significantly increased (+1.9 [0.8;3.0]95%CI hours/day; p<0.001) from baseline to follow-up
- Corresponding decreased time in hyperglycemia (-1.8 [-3.0;-0.6]95%CI hours/day; *p*=0.003)
- Decreased L2 hypoglycemia (-0.3 [-0.6;-0.1]95%CI hours/day; *p*=0.005), and no change in time in L1 hypoglycemia.
- Meals without bolus insulin within -15 and +60 minutes from meal start decreased by 30% over study (*p*=0.002).
- Study showed potential benefit on glycemic control and dosing behavior with reliable insulin dose data from connected pen in those with T1D.

Adolfsson P et al. *Diabetes Technology & Therapeutics*. 2020;10.1089/dia.2019.0411.

CGM & Insulin-dosing Algorithms

- Hybrid closed loop systems combining CGM data, insulin-dosing algorithms and insulin pumps have demonstrated improved time in range and reduced hypoglycemia
- CGM also associated with improved A1C in T2D MDI pts[1]
- Smart connected pens associated with increased time in range and decreased missed bolus insulin injections in MDI T1D pts[2]
- In future “smart insulin pen or cap for pen” combined with CGM data and insulin dosing algorithm will provide dosing recommendations to MDI treated patients on their smartphone.

1. Beck R W et al. *Ann Intern Med.* 2017;167(6): 365-374.
2. Adolfsson P et al. *Diabetes Technology & Therapeutics.* 2020;10.1089/dia.2019.0411

Therapeutic Inertia in Diabetes Care: A Call for Action in Clinical Practice - Summary

- Prevalence of diabetes continues to increase
- State of diabetes health care quality needs improvement
- Therapeutic Inertia - Clinical Inertia contribute to suboptimal diabetes care
- Decreased adherence is component of therapeutic inertia and hypoglycemia in insulin treated Individuals is a significant contributor
- Reduced hypoglycemia is seen with longer acting basal insulin analogues and in those with T2D when BI is combined with GLP-1 receptor agonists vs. basal bolus therapy
- Strategies to address Therapeutic Inertia may include
  - Timely intensification of and deintensification of diabetes medications
  - Increased use of CGM improve time in range and decrease hypoglycemia
  - Targeted intensive insulin-adherence interventions
- Clinicians, patients, health systems, payers, and industry entities developing diabetes medications, devices, and other products all can play a role in reducing Therapeutic Inertia

Consider these practice changes. Which ones will you make?

- Select insulin therapies taking into account patient-specific characteristics.
- Actively engage patients in ongoing discussions about the benefits of insulin therapies.
- Educate team members about the clinical profiles of currently available insulin products with respect to dosing, variability, volume, and safety.
- Educate team members about best practices in initiating insulin therapy.
- Educate team members on strategies for managing patients who exhibit psychological insulin resistance.
- Consider dose adjustments in patients who are non-adherent or are prone to clinical inertia.