

Diabetes Updates " Collaboration in Action"



Indiana Academy of Nutrition and Dietetics
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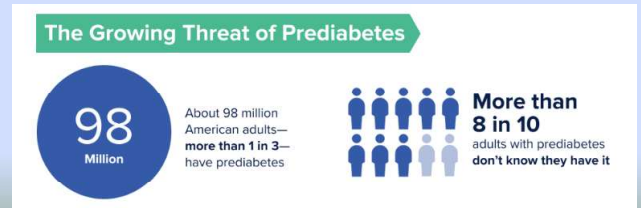
Disclosure

- Novo Nordisk Speakers Bureau

Objectives

- Review the impact of diabetes in the United States
- Learn about the main oral and injectable diabetes medications with emphasis on general adverse reactions and patient counseling tips
- Learn about some weight management medications that help reduce potential risks of diabetes
- Review the 2024 American Diabetes Association's general recommendations for medical management of patients with diabetes

National Diabetes Estimates



CDC 2023 National Diabetes Statistics Report

National Diabetes Estimates

- The 8th leading cause of death in the US
 - Risk of early death for adults with diabetes is **60% higher** than for adults without diabetes



CDC 2023 National Diabetes Statistics Report

National Diabetes Estimates

Cost burden in the US:



CDC 2023 National Diabetes Statistics Report

Epidemiology

US: Prevalence of obesity from 1999-2000 was 30.5%
 US: Prevalence of obesity form from 2017-2020 was 41.9%

Indiana is 5th in the nation for obesity at 36.8%

Obesity affects more patient groups than others

Non-Hispanic Black adults 49.6%
Hispanic adults 44.8%
Non-Hispanic white adults (42.2%) and Asian adults 17.4%

CDC: Overweight and Obesity -Adult Obesity Facts

Diagnosis of obesity can lead to “obesity associated conditions” (OAC)



T2DM: Type 2 Diabetes, HLD: Hyperlipidemia, CVD: Cardiovascular disease, NAFLD: Non-alcoholic fatty liver disease, PCOS: Polycystic ovary syndrome, OSA: obstructive sleep apnea, GERD: Gastroesophageal reflux disease

AAACE/ACE Obesity CPG, Endocr Pract. 2016;22

Is Weight Loss Essential?

- **Diabetes Prevention Program: weight loss most important factor to prevent type 2 diabetes (↓ 58%)**
- **Goal of loss of 5-7% of body weight**
- **Every kg (2.2 lb) lost ↓ diabetes risk by 16%**



Hamman RF et al. *Diab. Care*, 29:2102-2107, 2006

“Weighing” the options

	Overweight	Obese	Severely Obese
BMI	≥ 25 + OAC*	≥ 30 or ≥ 27 with OAC*	≥ 40 or ≥ 35 with OAC*
Physical activity	✓	✓	✓
Nutrition modification	✓	✓	✓
Behavioral modification	✓	✓	✓
Medications		✓	✓
Surgery			✓

*Obesity Associated Conditions = OAC = HTN, HLD, T2DM, OSA, pre-diabetes, osteoarthritis, PCOS, NAFLD

AAACE/ACE Obesity CPG, Endocr Pract. 2016;22

Physiologic Responses to Weight loss

Within 5 years most patients regain >50% of the weight that was lost on therapy

Monetsi et al. *Diabetes Metab Syndr Obes*. 2016;9:37-46

Rx Medications Used for Weight Reduction

FDA Approved

- Sympathomimetics:
 - Phentermine (IV)*
 - Diethylpropion (IV)*
 - Phendimetrazine (III)*
 - Benzphetamine (III)*
- Phentermine/ Topiramate (IV)
- Naltrexone/ Bupropion
- Liraglutide 3.0 mg
- Semaglutide 2.4 mg

Off-Label

- Metformin
- GLP-1 agonists: Liraglutide 1.8 mg, Semaglutide, Exenatide
- GIP/GLP-1 agonist: Tirzepatide
- SGLT2 inhibitors
- Topiramate
- Zonisamide
- Bupropion
- Naltrexone

*Approved for short-term use. Long-term use is Off-Label. Know your state laws

Drugs Approved for Type 2 Diabetes With or Without Obesity Indication

Drug Name (Alternate Name)	Route of Administration & Frequency	Mechanism of Action	Development Phase	Therapeutic Area
Tirzepatide ^{1,2} (LY3298176)	SC injection once weekly	Dual GIP/ GLP-1 RA	Phase 3	Obesity
Tirzepatide ³ (Mounjaro)			FDA approved	T2D
Semaglutide ^{1,2,11} (Unnamed)	PO once daily	GLP-1 RA	Phase 3	Obesity
				T2D
Semaglutide ⁴ (Byetta)			FDA approved	T2D
Semaglutide ² (Wegovy)	SC injection once weekly	GLP-1 RA	FDA approved	Obesity
Semaglutide ³ (Ozempic®)				T2D
Liraglutide ² (Saxenda)	SC injection once daily	GLP-1 RA	FDA approved	Obesity
Liraglutide ⁴ (Victoza)				T2D
Dulaglutide ^{2,4} (Trulicity)	SC injection once weekly	GLP-1 RA	FDA approved	T2D
Exenatide ² (Byetta)	SC injection twice daily	GLP-1 RA	FDA approved	T2D
Exenatide ^{2,3} (Bydureon BCise)	SC injection once weekly			

Abbreviations: GIP, gastric inhibitory peptide; GLP-1 RA, glucagon-like peptide 1 receptor agonist; N/A, not applicable; PO, per oral/orally; SC, subcutaneous; T2D, type 2 diabetes.

ADA Standards of Medical Care in Diabetes - 2024



<https://care.diabetesjournals.org>

Available in an app – IOS/Android or a web app

Beginning with the 2018 ADA Standards of Medical Care in Diabetes, the Standards document became a “living” document where notable updates are incorporated into the Standards

“The Standards of Care recommendations are not intended to preclude clinical judgment and must be applied in the context of excellent clinical care, with adjustments for individual preferences, comorbidities, and other patient factors.”

American Diabetes Association; Standards of Medical Care in Diabetes—2024. *Diabetes Care* 1 January 2024; 47 (Supplement_1)

Classification of Diabetes

- **Insulin-Dependent Diabetes Mellitus (Type I)**
 - High anti-beta cell antibodies
 - Low plasma insulin concentration (determined by C-peptide levels)
 - Usually lean and young patients but this trend is changing
- **Non-Insulin-Dependent Diabetes Mellitus (Type II)**
 - Serum insulin levels normal or elevated but still have relative insulin deficiency
 - Metabolism does not respond properly to insulin= insulin resistance
 - Usually obese (60-90%) and older but lean patient trend is changing
 - Losing weight frequently brings glucose levels and insulin sensitivity back under control
 - Strong genetic linkage

Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes – 2024. *Diabetes Care* 2023;47(S20-S42)

Classification of Diabetes (Cont.)

- **Type 1.5 Diabetes** (also known as slow onset type I or latent autoimmune diabetes in adults)
 - Patients do not immediately require insulin for treatment
 - Little or no resistance to insulin
 - Antibodies present (especially GAD65)
 - Can be easily misdiagnosed as Type II since patients are older and respond to oral medications except glitazones (since little or no insulin resistance) & usually have good C-peptide levels
- **Gestational Diabetes (GD)**
 - In most cases, slender and physically fit patients
 - Approximately 4% of all pregnancies according to ADA
 - 5-10% of women with GD are found to have type 2 diabetes
 - Women with GD have 20-50% chance to develop diabetes in the next 5-10 years
 - Screen women with GD at least every 3 years for diabetes/pre-diabetes

Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes – 2024. *Diabetes Care* 2023;47(S20-S42)

Criteria for the Diagnosis of Diabetes

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 the WHO, using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.*

OR

A1C $\geq 6.5\%$ (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

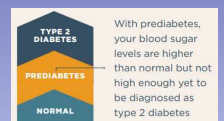
OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L).

*In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.

Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes – 2024. *Diabetes Care* 2023;47(S20-S42)

Pre-Diabetes



- Rapidly growing in prevalence in the U.S.
- 38% of adults ≥ 20 years have pre-diabetes

Test	Diabetes	Pre-diabetes
A1C	$\geq 6.5\%$	5.7-6.4%
Pre-prandial plasma glucose (fasting for 8 hours)	≥ 126 mg/dL	100-125 mg/dL
2-hour peak postprandial plasma glucose	≥ 200 mg/dL during OGTT (75-g)	140-199 mg/dL
Classic symptoms of hyperglycemia + random PG ≥ 200 mg/dL		

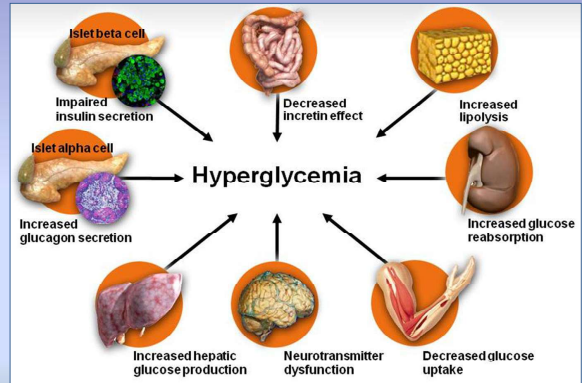
Prevention of Delay of Type 2 Diabetes and Associated Comorbidities: Standards of Medical Care in Diabetes – 2024. *Diabetes Care* 2023;47(S43-S51)

Pre-Diabetes Interventions

- Consider starting metformin in patients with pre-diabetes who:
 - BMI ≥ 35 kg/m²
 - Age < 60 years
 - Women with history of gestational diabetes
- Monitor at least annually for the development of type 2 diabetes
- Recommend a goal to achieve and maintain 7% loss of initial body weight

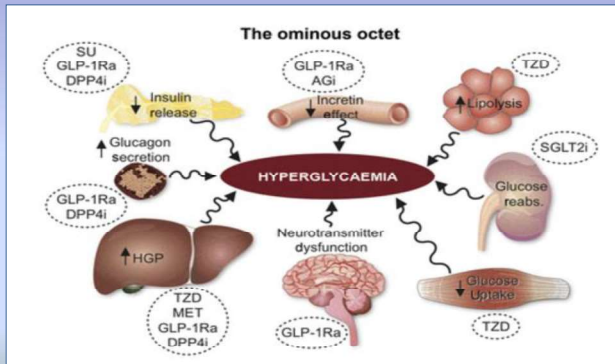
Prevention of Delay of Type 2 Diabetes and Associated Comorbidities: Standards of Medical Care in Diabetes – 2024. Diabetes Care 2023;47(S43-S51)

Pathogenesis of Type 2 Diabetes



DeFronzo RA. Diabetes Care. 2009;58:773-95.; DeFronzo RA, et al. Diabetes Care. 2013;36(2):S127-S138.

Medications sites of action



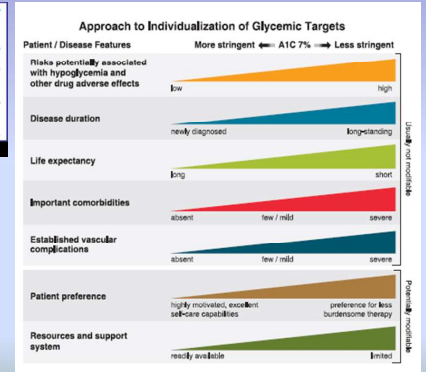
DeFronzo RA. Diabetes Care. 2009;58:773-95.; DeFronzo RA, et al. Diabetes Care. 2013;36(2):S127-S138.

Approach to Individualization of Glycemic Targets

A1C	<7.0% (53 mmol/mol)*#
Preprandial capillary plasma glucose	80-130 mg/dL* (4.4-7.2 mmol/L)
Peak postprandial capillary plasma glucose†	<180 mg/dL* (10.0 mmol/L)

HgbA1c & blood glucose correlation:
 • estimated average glucose = $(28.7 \times A1c) - 46.7$

- 6% = 126 mg/dl
- 7% = 154
- 8% = 183
- 9% = 212, etc.



Glycemic targets: Standards of Medical Care in Diabetes – 2024. Diabetes Care 2023;47(S111-S125)

Clinical Targets For CGM Monitoring Data Interpretation

AGP Report

Name: _____
MRN: _____

GLUCOSE STATISTICS AND TARGETS

14 days % Sensor Time

Glucose Ranges	Targets (% of Readings (Time/Day))
Target Range 70-180 mg/dL (3.9-8.0 mmol/L)	Greater than 70% (10h 48min)
Below 70 mg/dL	Less than 4% (56min)
Below 54 mg/dL	Less than 1% (14min)
Above 180 mg/dL	Less than 25% (9h)
Above 250 mg/dL	Less than 5% (1h 12min)

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

Average Glucose
Glucose Management Indicator (GMI)
Glucose Variability
 Defined as percent coefficient of variation (%CV); target $\leq 36\%$

TIME IN RANGES

Type 1 & Type 2 Diabetes

Glucose Range	Target
>250 mg/dL (13.9 mmol/L)	<5%
>180 mg/dL (10.0 mmol/L)	<25%
Target Range 70-180 mg/dL (3.9-8.0 mmol/L)	>70%
<70 mg/dL (3.9 mmol/L)	<4%
<54 mg/dL (3.0 mmol/L)	<1%

AGP: Ambulatory Glucose Profile

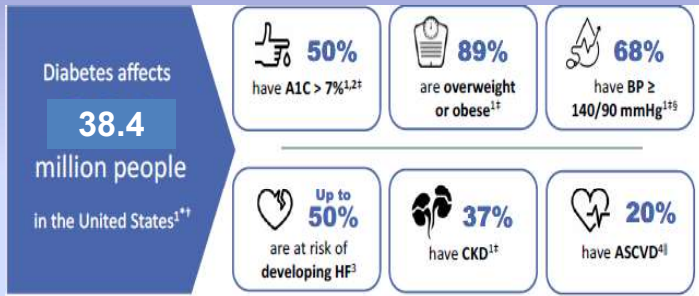
Diabetes Technology: Standards of Medical Care in Diabetes – 2024. Diabetes Care 2023;47(S126-S144)

Diabetes Management

- Control of A1c, fasting glucose (FG) and postprandial glucose levels (PPG) (*DECODE study showed that PPG is more predictive than A1c and FG for CV risk**)
- Hypertension-goal is <130/80 mmHg
- Dyslipidemia (General Guidelines):
 - *LDL < 70 mg/dl (reduction from baseline of $\geq 50\%$)
 - *HDL men > 40 mg/dl, women > 50 mg/dl
 - *Triglycerides < 150 mg/dl

Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE)

Type 2 diabetes is Associated with Multiple Comorbid Conditions



Prevention of Diabetes will help prevent many other diseases

CDC. National Diabetes Statistics Report 2022

Oral Diabetes Medications

Class/Main Action	Name(s)	Daily Dose Range	Considerations
Biguanides • Decreases hepatic glucose output • First-line medication at diagnosis of type 2 diabetes Benefits: lowers cholesterol, no hypoglycemia or weight gain, cheap. Approved for pediatrics, 10 yrs + Lowers A1C 1.0-2.0%	Metformin (Glucophage) Riomet (liquid metformin)	(BID dosing) 500-2550 mg 500 mg/5 mL	Side effects: nausea, bloating, diarrhea, B12 deficiency Use XR formulation and take with meals to minimize GI side effects
	Extended Release-XR (Glucophage XR) (Glumetza) (Fortamet)	(once daily) 500-2000 mg 500-2000 mg 500-2500 mg	Obtain eGFR before initiation • eGFR 30 to 45: initiation not recommended, however 500 mg once daily with evening meal, titrated to 500 mg twice daily, if tolerated → monitor renal function closely • eGFR <30: do not use Dye study: eGFR <60, stop taking metformin at the time of contrast administration; normal renal function, contrast-induced nephropathy is very low
Sulfonylureas • Stimulates sustained insulin release Lowers A1C 1.0-2.0%	Glyburide (DiaBeta) (Glynase)	1.25-20 mg/day 0.75-3 mg/day	Side effects: hypoglycemia (glyburide) and weight gain Administered with the first main meal Low cost
	Glipizide (Glucotrol) (Glucotrol XL)	2.5-40 mg/day 2.5-20 mg/day	
	Glimepiride (Amaryl)	1-8 mg/day	

Lexicomp (2024)

Oral Diabetes Medications (Cont.)

Class/Main Action	Name(s)	Daily Dose Range	Considerations
SGLT2 Inhibitors "Glucoretic" • Decreases glucose reabsorption in kidneys Lowers A1C 0.6-1.5% Lowers wt 1-3 lbs	Canagliflozin* (Invokana)	100-300 mg daily Contraindicated eGFR <30	Side effects: hypotension, UTIs, increased urination, genital infections, ketoacidosis Obtain eGFR before initiation • See package insert for dosing based on eGFR *Canagliflozin, Dapagliflozin, & Empagliflozin: • Reduce risk of CV death, heart failure, and preserve long-term kidney function Benefits: no hypoglycemia
	Dapagliflozin* (Farxiga)	5-10 mg daily Contraindicated eGFR <45	
	Empagliflozin* (Jardiance)	10-25 mg daily Contraindicated eGFR <30	
	Ertugliflozin (Steglatro)	5-15 mg daily Contraindicated eGFR <45	
	Bexagliflozin (Brenzavvy)	20 mg daily Contraindicated eGFR <30	
DPP-4 "Incretin Enhancers" • Prolongs action of gut hormones • Increases insulin secretion • Delays gastric emptying Lowers A1C 0.6-0.8%	Sitagliptin (Januvia)	25-100 mg daily- eliminated via kidney*	*see package insert for altered kidney function dosing
	Saxagliptin (Onglyza)*	2.5-5 mg daily- eliminated via kidney* and feces	Side effects: headache and flu-like symptoms
	linagliptin (Trazienta)	5 mg daily- eliminated via feces	Can cause severe, disabling joint pain. Contact MD, stop med. Report signs of pancreatitis.
	Alogliptin (Nesina)*	6.25-25 mg daily- eliminated via kidney*	+Saxagliptin and alogliptin can increase risk of heart failure. Notify MD for shortness of breath, edema, weakness, etc. No wt gain or hypoglycemia.

Lexicomp (2024)

Oral Diabetes Medications (Cont.)

Class/Main Action	Name(s)	Daily Dose Range	Considerations
Thiazolidinediones "TZDs" • Increases insulin sensitivity	pioglitazone (Actos)	15 – 45 mg daily	Black Box Warning: TZDs may cause or worsen CHF. Monitor for edema and weight gain. Increased peripheral fracture risk. Actos may increase risk of bladder cancer. Lower A1c 0.5% – 1.0% Start low dose, increase at 4-8 wk intervals to decrease GI effects. Caution with liver or kidney problems. In case of hypo, treat w/ glucose tabs. Lower A1c 0.5–1.0%.
	rosiglitazone (Avandia)	4 – 8 mg daily	
Glucosidase Inhibitors • Delays carb absorption	acarbose (Precose)	25 – 100 mg w/meals;	Lower A1c 0.5–1.0%.
	miglitol (Glyset)	300 mg max daily dose	
Meglitinides • Stimulates rapid insulin burst	repaglinide (Prandin)	0.5 – 4 mg w/meals (metabolized in liver)	Take before meals. Side effects may include hypoglycemia and weight gain. Lower A1c 1.0% – 2.0%.
	nateglinide (Starlix)	60 – 120 mg w/meals (eliminated via kidney)	
Dopamine Receptor Agonists • Resets circadian rhythm	bromocriptine mesylate— Quick Release "QR" (Cycloset)	1.6 to 4.8 mg a day (each tab 0.8 mg)	Take within 2 hrs of waking. Side effects: nausea, headache, fatigue, hypotension, syncope, somnolence. Lower A1c 0.5% – 0.9%.
Bile Acid Sequestrants • Decreases cholesterol / BG levels.	Colesevelam HCL (Welchol)	Up to six (6) 625 mg pills (3 tabs am, 3 tabs pm) 3.75gm packet in 4-8 ounces of fluid	Do not use if history of bowel obstruction, triglycerides >500, or pancreatitis. Can decrease absorption of certain meds, soluble vitamins. Lowers LDL by 15-30%. Side effects GI in nature. Lower A1c 0.5%

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Combo Oral Medications

Medications	Doses in mg	Medications	Doses in mg	Medications	Doses in mg
Trijardy XR (3 meds) empagliflozin linagliptin metformin XR	5 – 25 2.5 – 5 1000	Janumet (sitagliptin/ metformin)	50/500 50/1000	Prandimet (repaglinide/ metformin)	1/500 2/500
ACTOplus Met* (pioglitazone/ metformin)	15/500 15/850	Janumet XR (sitagliptin/ metformin)	50/500 50/1000 or 100/1000	Qtern (saxagliptin / dapagliflozin)	5/10
ACTOplus Met XR (pioglitazone/ metformin)	15/1000 30/1000	Jentaduet (linagliptin/ metformin)	2.5/500 2.5/850 or 2.5/1000	Segluromet (ertugliflozin/ metformin)	2.5/500 or 2.5/1000 or 7.5/500 or 7.5/1000
Duetact* (pioglitazone/ glimepiride)	30/2 30/4	Kazano (alogliptin/ metformin)	12.5/500 12.5/1000	Steglujan (ertugliflozin/ sitagliptin)	5/100 or 15/100
Glucovance* (glyburide/ metformin)	1.25/250 2.5/500 5/500	Kombiglyze XR (onglyza/metformin XR)	2.5/1000 5/600 or 5/1000	Synjardy (empagliflozin/ metformin)	5/500 or 12.5/500 5/1000 or 12.5/1000
Glyxambi (empagliflozin and linagliptin)	10/5 25/5	Metaglip* (glipizide/ metformin)	2.5/250 2.5/500 or 5/500	Synjardy XR (empagliflozin/ metformin XR)	5/1000 or 10/1000 12.5/1000 or 25/1000
Invokamet (canagliflozin/ metformin)	50/500 or 50/1000 150/500 or 150/1000	Oseni (alogliptin/ pioglitazone)	12.5/15 or 25/15 12.5/30 or 25/30 12.5/45 or 25/45	Xiadduo XR (dapagliflozin/ metformin)	5/500 or 10/500 5/1000 or 10/1000

Lexicomp (2024)

GLP-1 Agonists & Non-insulin Injectables

Class/Main Action	Name	Dose Range	Considerations
GLP-1 Receptor Agonist (GLP-1 RA) "Incretin Mimetic" • Increases insulin release with food • Slows gastric emptying • Promotes satiety • Suppresses glucagon	exenatide (Byetta)	5 and 10 mcg BID	Side effects for all: Nausea, vomiting, weight loss, injection site reaction. Report signs of acute pancreatitis (severe abdominal pain, vomiting), stop med. Renally excreted. Black box warning: Thyroid C-cell tumor warning for exenatide XR, liraglutide, dulaglutide, and semaglutide (avoid if family history of medullary thyroid tumor). *Significantly reduces risk of CV death, heart attack, and stroke. Lower A1c 0.5 – 1.6% Weight loss of 1.6 to 6.0kg†
	exenatide XR (Bydureon)	2 mg 1x a week Pen injector - Bydureon BCise	
	liraglutide (Victoza)*	0.6, 1.2 and 1.8 mg daily Approved for pediatrics 10 yrs +	
	dulaglutide (Trulicity)*	0.75, 1.5, 3.0 and 4.5 mg 1x a week pen injector	
	lixisenatide (Adlyxin)	10 mcg 1x a day for 14 days 20 mcg 1x day starting day 15	
	semaglutide (Ozempic)**	0.5 and 1.0 mg 1x a week pen injector	
Amylin Mimetic • Slows gastric emptying • Suppresses glucagon	(Rybelsus) Oral tablet	3, 7, and 14 mg daily in a.m. Take on empty stomach w/H2O sip	Lower A1c 0.5 – 1.6% Weight loss of 1.6 to 6.0kg† For Type 1 or 2 on insulin. Severe hypoglycemic risk, decrease insulin dose when starting. Side effects: nausea, weight loss. Lower A1c 0.5 – 1%
	pramlintide (Symlin)	Type 1: 15 - 60 mcg; Type 2: 60 - 120 mcg immediately before major meals	

Lexicomp (2024)

GLP-1/GIP Agonist

Class/Main Action	Name	Dose Range	Considerations
GLP-1/GIP (glucose-dependent insulinotropic polypeptide) "Incretin Mimetic" <ul style="list-style-type: none"> Increases insulin release with food Slows gastric emptying Promotes satiety Glucagonotropic Glucagonostatic 	Tirzepatide (Mounjaro)	2.5-15 mg subcutaneous weekly	US Boxed Warning: risk of thyroid c-cell tumors (avoid use if family or personal history) Side effects: nausea, vomiting, weight loss, injection site reaction, pancreatitis (discontinue medication immediately) Lowers A1C 0.5-1.6% Weight loss of 1.6-6 kg

Lexicomp (2024)

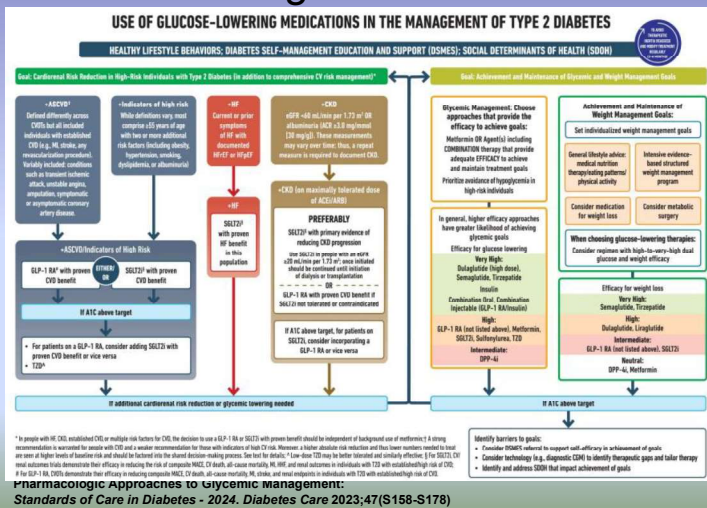
Insulin/GLP-1 Combination

Name	Combines	Considerations
iDGLira* Xultophy 100/3.6	Insulin degludec (IDeg or Tresiba) Ultra long insulin + Liraglutide (Victoza) GLP-1 Receptor Agonist (GLP-1 RA)	Xultophy 100/3.6 pre-filled pen – 100 units IDeg / 3.6 mg liraglutide per mL Once daily injection – Dose range 10 to 50 = 10 – 50 units IDeg + 0.36 – 1.8 mg liraglutide Recommended starting dose: • 16 iDGLira (= 16 units IDeg + 0.58 mg liraglutide) Titrate dose up or down by 2 units every 3-4 days to reach target. Supplied in package of five single-use 3mL pens. Once opened, good for 21 days.
iGlarLixi* Soliqua 100/33	Insulin glargine (Lantus) Basal Insulin + Lixisenatide (Adlyxin) GLP-1 Receptor Agonist	Soliqua 100/33 Solostar Pen = 100 units glargine / 33 µg lixisenatide per mL Once daily injection an hour prior to first meal of day. Dose range 15 – 60 = 15-60 units glargine + 5 – 20µg lixisenatide Recommended starting dose: • 15 units for pts not controlled on 30 units basal insulin or GLP 1 RA • 30 units for pts not controlled on 30-60 units basal insulin or GLP-1 RA Titrate dose up or down by 2-4 units every week to reach target. Supplied in package of five single-use 3mL pens. Once opened, good for 14 days.

*Discontinue basal Insulin /GLP-1 RA therapy before starting. If dose missed, resume with next usual scheduled dose.

Lexicomp (2024)

ADA 2024 Algorithm DM Meds



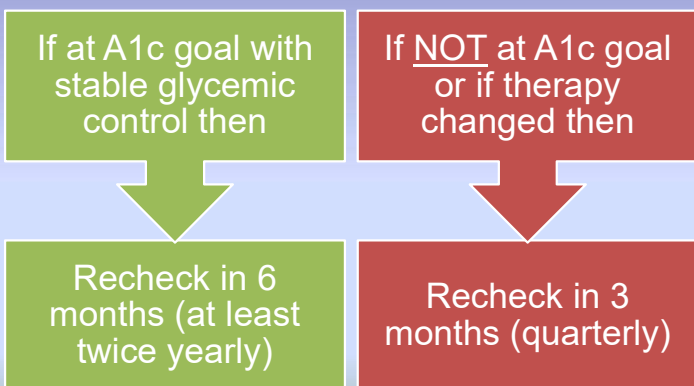
Benefits of Reducing A1c by 1%

- Type I diabetes (DCCT)
 - 32% decrease in risk for retinopathy
 - 20% -27% decrease in risk for nephropathy
 - 30% decrease in risk for neuropathy
- Type II diabetes (UKPDS)
 - 10% decrease in risk of diabetes-related death
 - 6% decrease in all-cause mortality
 - 16% decrease in risk for MI
 - 25% decrease in microvascular complications

DCCT = Diabetes Control and Complications Trial

UKPDS = United Kingdom Prospective Diabetes Study

When to Recheck the A1c



American Diabetes Association. Standards of medical care in diabetes—2024. Diabetes Care. 2023;47(S1-S313)

Cholesterol Medications - Statins

- Total cholesterol goal is < 200, LDL < 70, HDL for men > 45, for women > 55 and triglycerides < 150
- Have been shown to cut down on the incidence of heart attacks and strokes in patients with diabetes
- May delay the initiation of insulin in Type 2 diabetes
- Take at bedtime and **avoid grapefruit and grapefruit juice**
- Monitor liver function tests initially and at least annually
- Side effects to tell the doctor about include: muscle weakness, skin rash, nausea, vomiting, diarrhea and loss of appetite

Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes – 2024. Diabetes Care 2023;47(S52-S76)

Blood Pressure Medications

- Blood pressure goal is $\leq 130/80$ mmHg
- Blood pressure control has shown to decrease cardiovascular disease, stroke, and kidney damage in diabetics
- Lifestyle changes may be adequate for some
- Some diabetics are started on blood pressure medications called angiotensin-converting enzyme (ACE) inhibitors **or** Angiotensin Receptor Blockers (ARBs) which offer kidney protection as well. ****CONTRAINDICATED IN PREGNANCY!****
- There are many different classes of blood pressures medications that diabetics may be on concomitantly

Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes – 2024. Diabetes Care 2023;47(S52-S76)

Recommendations: Medical Nutrition Therapy (MNT)

- Individuals who have prediabetes or diabetes should receive **individualized** MNT as needed to achieve treatment goals, preferably provided by a registered dietitian familiar with the components of diabetes MNT
- 5% weight loss recommended for overweight patients
- In general:
 - Carbs 45-65% of total daily calories (controversial)
 - Fats 20-35% of total daily calories (<7% saturated)
 - Protein 15-20 % (kidney disease <10%)
- Limit sodium consumption to at least 2,300 mg/day

Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes: Standards of Medical Care in Diabetes – 2024. Diabetes Care 2023;47(S145-S157)

ADA Recommendations: Physical Activity

- Advise people with diabetes to perform at least 150 min/week of moderate-intensity aerobic physical activity (50–70% of maximum heart rate), spread over at least 3 days per week with no more than 2 consecutive days without exercise
- In absence of contraindications, people with diabetes should be encouraged to perform resistance training at least twice per week

Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes: Standards of Medical Care in Diabetes – 2024. Diabetes Care 2023;47(S145-S157)

Additional Recommended Screenings

Urinary Albumin	Eye Exam	Foot Exam
<ul style="list-style-type: none"> • Assess for nephropathy • Screen initially and then once annually • 30-300 mg/g creatinine = microalbuminuria • >300 mg/g creatinine = macroalbuminuria 	<ul style="list-style-type: none"> • Assess for retinopathy • Screen initially and then every 1-2 years • At least annually if any degree of diabetic retinopathy noted 	<ul style="list-style-type: none"> • Assess for neuropathy/ulceration • Screen initially and then once annually • Temperature/pinprick sensation and vibration sensation using a 128-Hz tuning fork

Retinopathy, Neuropathy, and Foot Care: Standards of Medical Care in Diabetes – 2024. Diabetes Care 2023;47(S231-S234)

Smoking Cessation

- Ask about readiness to quit at EVERY ENCOUNTER
- Counseling and offer for treatment should be included as a routine component of diabetes care
- Advise all patients not to use cigarettes, other tobacco products, or e-cigarettes
- Smokers with diabetes have a heightened risk of CVD, premature death, microvascular complications, and worse glycemic control

Facilitating Behavior Change and Well-being to Improve Health Outcomes: Standards of Medical Care in Diabetes – 2024. Diabetes Care 2023;47(S77-S110)

Over the Counter Medications

- Use only as directed
 - If product needed more than 5-7 days, notify your doctor
 - Decongestants (pseudoephedrine, Sudafed) and NSAIDs
 - Prolonged use can increase blood pressure and decrease circulation
- Watch for sugar and alcohol content-- especially in cough syrups!
 - Many products are available sugar free and alcohol free--Diabetic Tussin & Codimal DM

Herbals and Nutraceuticals

- Consult doctor prior to use
- Check glucose before and after you take, routinely for first few weeks, then periodically
- Use caution with all herbals, especially:
 - Ginseng
 - Ginger
 - Glucosamine
 - Garlic
 - Gingko
 - Ma Huang or Ephedra
 - Nettle
 - Cinnamon



Diabetes in Hospitalized Patients

- Prevalence 13-26%
 - 30-50% in acute MI acute stroke patients
- In 2017, 14 million visits to the ED with diabetes as the primary diagnosis
- Up to 38% of hospitalized patients experience hyperglycemia
- Inpatient hyperglycemia is associated with
 - Longer hospital stays
 - Higher admission rates to intensive care
 - More patients requiring transitional or nursing home care
- **Up to 36% of patients with diabetes are first diagnosed in hospital**

Rubens M, et al. Recent Trends in Diabetes-Associated Hospitalizations in the United States. *J Clin Med.* 2022 Nov 9;11(22):6636

Insulin Fundamentals

Think about insulin therapy as having three components:

1. **Basal insulin** : what you need when not eating (between meals)
2. **Prandial insulin**: to cover food
3. **Correction insulin**: to fix abnormal glucose levels

Characteristics of Most Common Hospital Formulary Insulin

Rapid acting Insulin such as **Novolog, Humalog or Apidra**
Onset: 10-15 min Peak: 30-90 min Duration: 6-8 hrs

Fast acting Insulin such as **Novolin R or Humulin R**
Onset : 30 min Peak : 2-4 hrs Duration 8-12 hrs

Intermediate Acting Insulin such as **Novolin N or Humulin N**
Onset :1-2 hrs Peak: 4-12 hrs Duration 18-24 hrs

Basal (long acting Insulin) such as **Lantus (Gargine) or Levemir (Detemir)**
Onset: 1-2 hrs No Peak Duration: Up to 24 hrs

Mixed Insulin such as **Humulin or Novolin 70/30, Novolog Mix 70/30, Humalog 75/25, Humalog 50/50**

Concentrated Insulins

- **Tresiba** (insulin degludec)
 - Long acting, once-a-day injection
 - Flexible dosing time
 - Comes in standard (U-100) and concentrated pens (U-200)
- **Ryzodeg** (70% insulin degludec + 30% insulin aspart)
 - Tresiba + a rapid acting meal time insulin
- **Toujeo SoloStar** (insulin glargine) 300 units/ml
 - Long acting
 - IU Health: Converted to Lantus at 80% of the dose if on Toujeo at home
 - Same insulin found in Lantus
 - Smaller volume to be administered
- **Humalog U-200** (200 units/ml): Rapid-acting



- **Insulin U-500 Pen** (Humulin R)



Lexicomp (2024)

Human Insulin Inhalation Powder

- Rapid acting, meal time inhaled insulin for type 1 and 2
- Prior to administration, assess lung function including spirometry (FEV1) in all patients
- Afrezza® is contraindicated in patients with chronic lung disease (eg asthma or COPD); risk of acute bronchospasm



Afrezza PI, 2018

Insulins

Action	Insulin Name	Onset	Peak	Effective Duration	Considerations
Bolus	Very Rapid Acting Analogs Aspart (Fiasp)	2.5 min	~60 min	3-5 hours	Bolus insulin lowers after-meal glucose. Post meal BG reflects efficacy.
	Lispro-aabc (Lyumjev)	1 min	~60 min	4-5 hours	
	Rapid Acting Analogs Aspart (Novolog)	5 - 15 min	30 - 90 min	< 5 hrs	Basal insulin controls BG between meals and nighttime. Fasting BG reflects efficacy.
	Lispro (Humalog*/ Admelog) Glulisine (Apidra)				
Short Acting Regular*	30 - 60 min	2 - 3 hrs	5 - 8 hrs		
Basal	Intermediate NPH	2 - 4 hrs	4 - 10 hrs	10 - 16 hrs	Side effects: hypoglycemia, weight gain. Typical dosing range: 0.5-1.0 units/kg body wt/day.
	Long Acting Detemir (Levemir)	3 - 8 hrs	No peak	6 - 24 hrs	
	Glargine (Lantus*/ Basaglar/Semglee) Degludec (Tresiba)*	2 - 4 hrs ~ 1 hr	No peak	20 - 24 hrs < 42 hrs	
Basal + Bolus	Intermediate + short Combo of NPH + Reg 70/30 = 70% NPH + 30% Reg 50/50 = 50% NPH + 50% Reg	30 - 60 min	Dual peaks	10 - 16 hrs	Discard open vials after 28 days. For pen storage guidelines, see package insert.
	Intermediate + rapid Novolog* Mix - 70/30 Humalog* Mix - 75/25 or 50/50	5 - 15 min		24 hrs	

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Lexicomp (2024)

Concentrated and Inhaled Insulin

Name/Concentration	Insulin/Action	Considerations
Humulin Regular U-500 • 500 units insulin/mL • KwikPen or Vial	Regular Bolus / Basal	5 x concentration of u-100 insulin. Indicated for pts taking 200+ units insulin daily. 3 mL Pen – Once opened, good for 28 days. 20 mL Vial – Once opened, good for 40 days. Use designated U-500 insulin syringe.
Humalog KwikPen U-200 200 units insulin/mL	Lispro (Humalog) Bolus	2 x concentration of u-100 insulin. 3 mL Pen. Once opened, good for 28 days
Toujeo Solostar U-300 Pen 300 units insulin/mL	Glargine (Lantus) Basal	3 x concentration of u-100 insulin 1.5 mL or 3 mL (Max Solostar) Pen.
Tresiba FlexTouch U-200 Pen 200 units insulin/mL	Degludec (Tresiba) Ultra basal	2 x concentration of u-100 insulin 3 mL Pen. Once opened, good for 8 weeks

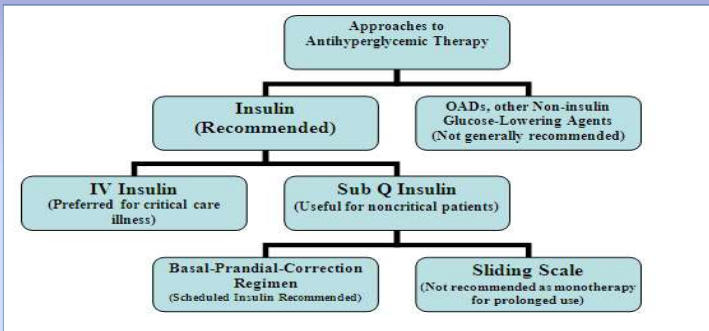
All concentrated insulin pens and the U-500 syringe automatically deliver correct dose (in less volume). No conversion, calculation or adjustments required. For example, if order reads 30 units, dial the concentrated pen to 30 units or draw up 30 units on the U-500 syringe. Important – never withdraw concentrated insulin from the pen using a syringe.

Inhaled Insulin

Action	Insulin Name	Dose Range	Onset	Peak	Duration	Considerations
Bolus – Rapid-acting	Afrezza inhaled regular human insulin	4, 8, and 12 unit cartridges before meals	~ 12 min	35 - 45 mins	1.5 - 3 hrs	Assess lung function. Avoid in lung disease – bronchospasm risk. Side effects: hypo, cough, throat irritation.

Lexicomp (2024)

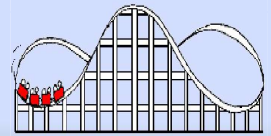
AACE/ADA Recommendations for Managing Patients With Diabetes in the Hospital Setting



1. Moghissi ES et al. Diabetes Care. 2009;32(6):1119-1131.
2. ADA. Diabetes Care. Diabetes Care. 2011 34:S11-S61.

The Dark Side of The Sliding Scale

- Problems:
 - Omits basal insulin requirements
 - Insulin does not work retroactively (treating hyperglycemia after it occurs instead of preventing it)
 - Does not account for mealtime calories
 - Grossly underestimates insulin requirements
- Benefits:
 - Very popular but hazards exceed the advantages of its convenience



AACE Inpatient Glycemic Control Resource.

AACE-ADA Consensus Statement on Inpatient Glycemic Control

Endocr Pract. 2009;15:353-69.
Diabetes Care. 2009;32:1119-31

AACE/ADA Consensus Statement

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN DIABETES ASSOCIATION CONSENSUS STATEMENT ON INPATIENT GLYCEMIC CONTROL

Etie S. Moghissi, MD, FACP, FACE¹; Mary T. Korytkowski, MD²; Monica DiNardo, MSN, CRNP, CDE³; Daniel Einhorn, MD, FACP, FACE⁴; Richard Hellman, MD, FACP, FACE⁵; Irl B. Hirsch, MD⁶; Silvio E. Inzucchi, MD⁷; Faramarz Ismaili-Beigi, MD, PhD⁸; M. Sue Kirkman, MD⁹; Guillermo E. Umpteierrez, MD, FACP, FACE¹⁰

ADA/AACE Target Glucose Levels in ICU Patients

- ICU setting:
 - Insulin infusion should be used to control hyperglycemia
 - Starting threshold of no higher than 180 mg/dl
 - Once IV insulin is started, the glucose level should be maintained between 140 and 180 mg/dl
 - Lower glucose targets (110-140 mg/dl) may be appropriate in selected patients

ADA/AACE Inpatient Task Force Endocrine Practice 2009; 15:1-17.

ADA/AACE Target Glucose Levels in Non-ICU Patients

- Non-ICU setting:
 - Pre-meal glucose targets <140 mg/dL
 - Random BG <180 mg/dL
 - To avoid hypoglycemia, reassess insulin regimen if BG levels fall below 100 mg/dL
 - Occasional patients may be maintained with a glucose range below or above these cut-points

Hypoglycemia= BG < 70 mg/dl
Severe hypoglycemia= BG < 40 mg/dl

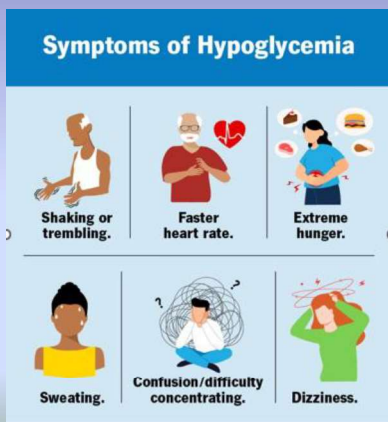
ADA/AACE Inpatient Task Force *Endocrine Practice* 2009; 15:1-17

Classification of Hypoglycemia

Classification of hypoglycemia		
Level	Glycemic criteria	Description
Hypoglycemia alert value (level 1)	≤70 mg/dL (3.9 mmol/L)	Sufficiently low for treatment with fast-acting carbohydrate and dose adjustment of glucose-lowering therapy
Clinically significant hypoglycemia (level 2)	<54 mg/dL (3.0 mmol/L)	Sufficiently low to indicate serious, clinically important hypoglycemia
Severe hypoglycemia (level 3)	No specific glucose threshold	Hypoglycemia associated with severe cognitive impairment requiring external assistance for recovery

Diabetes Care in the Hospital: Standards of Medical Care in Diabetes – 2024. *Diabetes Care* 2023;47(S295-S306)

Signs and Symptoms of Hypoglycemia



Treatment of Hypoglycemia

- The American Diabetes Association recommends the “15-15 rule” to treat an episode of mild to moderate hypoglycemia:
 - Eat or drink 15 grams of fast-acting carbs to raise your blood sugar.
 - After 15 minutes, check your blood sugar.
 - If it’s still below 70 mg/dL, have another 15 grams of fast-acting carbs.
 - Repeat until your blood sugar is at least 70 mg/dL.

Treatment:

- 1 small piece of fruit, such as half a banana.
- 4 ounces (half-cup) of juice or regular soda (not diet).
- 1 tablespoon of sugar, honey or syrup.
- 1 tube of instant glucose gel (check the instructions).
- 3 to 4 glucose tablets (check the instructions).
- Glucagon
- D50 (in hospital)

American Diabetes Association. Hypoglycemia (Low Blood Sugar). (<https://www.diabetes.org/diabetes/medication-management/blood-glucose-testing-and-control/hypoglycemia>) Accessed 3/5/2024

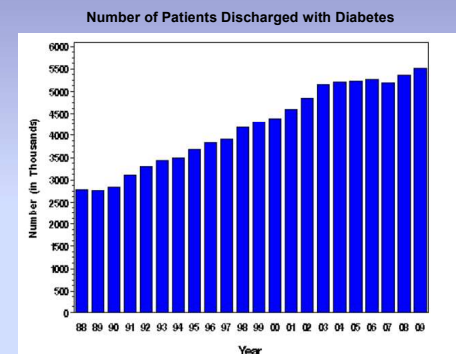
Hypoglycemia is Associated with Cardiovascular Complications

- Tachycardia and high blood pressure
- Myocardial ischemia
 - Silent ischemia, angina, infarction
- Cardiac arrhythmias
 - Transiently prolonged corrected QT interval,
 - Increased QT dispersion
- Sudden death

American Diabetes Association. Hypoglycemia (Low Blood Sugar). (<https://www.diabetes.org/diabetes/medication-management/blood-glucose-testing-and-control/hypoglycemia>) Accessed 3/5/2024

Diabetes at Discharge

- 23% of all discharges have diabetes diagnosis
- 8 – 9 million patients with diabetes discharged each year
- \$1 out of every \$3 Medicare dollars spent on diabetes care
- **1.7 – 1.9 million will return as an early readmission**



Rubin DJ, et al. Early readmission among patients with diabetes: a qualitative assessment of contributing factors. *J Diabetes Complications*. 2014 Nov-Dec;28(6):869-73

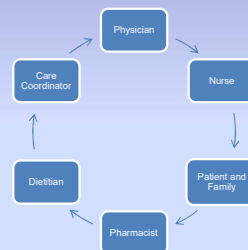
Preventing Readmission

- ADA Standards of Care
 - Discharge planning should begin upon admission and tailored to the individual patient at discharge
 - Medication reconciliation
 - Structured plan of care
 - Diabetes self-care education
 - Follow-up care planning
 - Individualize therapy
- Must provide comprehensive discharge planning via care coordination

Diabetes Care in the Hospital: Standards of Medical Care in Diabetes – 2024. *Diabetes Care* 2023;47(S295-S306)

Transitioning from Inpatient Stay

- Preparation from inpatient setting should begin at the time of admission
- Clear communication with outpatient providers is crucial
- Collaboration across the entire spectrum of the interdisciplinary team is critical for successful management



Diabetes Care in the Hospital: Standards of Medical Care in Diabetes – 2024. *Diabetes Care* 2023;47(S295-S306)

Key Patient Education Points Prior to Discharge

- How, when and what to expect from medications/insulin
- How and when to test blood glucose and target ranges to shoot for
- Basics of meal planning
- How to treat hypoglycemia
- Sick-day management plan
- Date/time of follow-up visits
- When and who to call if needed

Diabetes Care in the Hospital: Standards of Medical Care in Diabetes – 2024. *Diabetes Care* 2023;47(S295-S306)

Conclusion

- Diabetes is increasing at an alarming rate and is directly linked to the increased rate of obesity in the United States
- Diabetes imposes a huge economic burden on health care and hospitals
- Early identification of hyperglycemia is critical to improve outcomes
- Hypoglycemia can be very dangerous and should be avoided. Monitoring rates of hypoglycemia is KEY!!!
- Weight control medications particularly those that can help reduce major adverse cardiac events in patients with Diabetes can play a major role in Diabetes and obesity management.
- Collaboration between the inpatient health care practitioners and the ambulatory care practitioners is critical to ensure safe transition of care and reduce readmission rates
- Collaboration between all healthcare disciplines is very essential to care for patients with diabetes

Questions??



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Diabetes Updates “ Collaboration in Action”



Indiana Academy of Nutrition and Dietetics
Spring 2024 Conference

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