Advanced Clinical Management in Diabetes Care

Date: Thursday, September 29, 2016 | **When:** 1:00pm – 6:30 pm
Where: Marriott Bloomington-Normal Conference Center | **Contact:** kimc@ipha.org

Target Audience: Pharmacists in all practice settings

Overview

Diabetes now affects over 29 million patients in the United States, and nearly 8 million Americans are undiagnosed. A joint statement through the American Diabetes Association, the American Association of Diabetes Educators, and the Academy of Nutrition and Dietetics describes the role of diabetes self-management education/support and how pharmacists can assist patients in alternative settings to provide diabetes care.

On a daily basis, pharmacists in all practice settings work with patients to gain better control of specific short- and long-term goals of glycemic control. The world of diabetes management is always changing. This advanced program will provide you with up to date information about obesity, nutritional therapy and the technology and self-care advancements to manage diabetes. The program will also discuss the ever-expanding role of basal insulins and new evidence-based medicine when discussing novel diabetes treatment and clinical concerns.

Objectives

At the conclusion of this program, the pharmacist will be able to:

- Examine clinical recommendations for screening and treating patients who are overweight.
- Discuss updated cardiovascular outcomes and clinical concerns for non-insulin diabetes therapies.
- Identify indications for initiating basal insulin in persons with type 2 diabetes.
- Develop basal insulin regimens, based on patient-specific parameters, that align with current expert guidelines and/or clinical evidence.
- Discuss FDA regulations for blood glucose monitoring device standards.
- Compare and contrast glucose monitoring options and drug delivery devices available to aid in compliance and better self-efficacy of disease state control.
- Explore appropriate self-care counseling considerations for patients with diabetes.
- Review evidence based nutrition therapy recommendations for managing diabetes.
- Discuss the role of pharmacists in the delivery of the nutrition component of diabetes self-management education and support.

Registration Fee

Pharmacist: $125 (IPhA Member) - $345 (Non-member)

Student: $65 (IPhA Member) - $81 (Non-member

Registration includes dinner.
All non-member rates include a discounted one year IPhA membership.

ACPE® *The Illinois Pharmacists Association is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education.*

Advanced Clinical Management in Diabetes Care

Presented by:

The Role of Obesity Agents for Wellness
Dr. Jessica Kerr, PharmD, CDE
Associate Professor / Assistant Department Chair, Pharmacy Practice
Southern Illinois University Edwardsville School of Pharmacy

Basal Insulin: Initiation of Insulin and Advanced Management
Dr. Jennifer Rosselli, PharmD, BCPS, BCACP
Clinical Assistant Professor, Department of Pharmacy Practice
Southern Illinois University Edwardsville School of Pharmacy

Prevailing Clinical Concerns for FDA-Approved Diabetes Agents
Dr. Kate Petkewicz, PharmD, BCACP
Clinical Pharmacy Specialist, Ambulatory Care
Edward Hines Jr VA
Hoffman Estates Community Based Outpatient Clinic

Medical Nutritional Management for Patients with Type 2 Diabetes
Ms. Anne Daly, MS, RDN, BC-ADM, CDE
Director of Nutrition and Diabetes Education
Southern Illinois University School of Medicine Center for Family Medicine

Advancements in Technology and Incorporation of Self-Management Skills for Patients with Diabetes
Dr. Sneha Baxi Srivastava, PharmD, BCACP, CDE
Clinical Associate Professor
Chicago State University College of Pharmacy

Dr. Lalita Prasad-Reddy, PharmD, MS, BCPS, BCACP, CDE
Clinical Assistant Professor
Chicago State University College of Pharmacy

Continuing Pharmacy Education (CPE) Information and Activity Completion Requirements

Initial Release Date: September 29, 2016 Expiration Date: September 29, 2019
Target Audience: Pharmacists in all practice settings Activity Type: Application-based
Universal Activity Number: 0135-0000-16-007-L01-P Contact Hours: 5.0 (0.5 CEUs)

This activity is structured to meet application-based educational needs. An application-based activity applies to information learned in the time frame allotted. Information in application-type activities is based on evidence as accepted in the literature by the health care professions. Continuing pharmacy education (CPE) credit will be earned based on participation in individually accredited activities (this activity). Attendance and participation are required before obtaining CPE credit. Any individual who is more than 10 minutes late to an activity or leaves an activity early will not be granted CPE credit. This procedure will be strictly enforced, so please plan accordingly. Post test questions are not applicable to application-based activities; however, an evaluation must be completed.

This activity is accredited through ACPE for pharmacist continuing pharmacy education credit. If all requirements are met, participants will receive continuing pharmacy education credit in the following manner. Partial credit will not be awarded. Please allow 60 days for processing.

Pharmacists

CPE Monitor, a national, collaborative effort by ACPE and the National Association of Boards of Pharmacy (NABP) to provide an electronic system for pharmacists to track their completed CPE credits, went into effect on 01/01/2013. IPhA, as an ACPE-accredited provider, is required to report pharmacist CPE credit using this new tracking system. Pharmacist participants must provide their NABP e-Profile identification number and date of birth (in MMDD format) when they register for a CPE activity or complete activity evaluations. **It will be the responsibility of the pharmacist to provide the correct information (i.e., e-Profile identification number and date of birth in MMDD format). If this information is not provided, NABP and ACPE prohibit IPhA from issuing CPE credit.** Online access to their inventory of completed credits will allow pharmacists to easily monitor their compliance with CPE requirements and print statements of credit. Therefore, IPhA will not provide printed statements of credit to pharmacists. For additional information on CPE Monitor, including E-Profile set-up and its impact on pharmacists, go to www.nabp.net.

Refund Policy: Fees refunded, less $50 administrative fee, if cancelled by September 1, 2016. Cancellation must be received in writing to kimc@ipha.org.

Advanced Clinical Management in Diabetes Care

September 29, 2016
Marriott Bloomington – Normal Conference Center
Redbird E Room
1:00PM – 6:30PM

Agenda

1:00PM
Welcoming

1:15PM
The Role of Obesity Agents for Wellness
Jessica L. Kerr, PharmD, CDE
Shelley Monroe & Jordan Sinclair, SIUE PharmD Candidates

2:15PM
Advanced Clinical Medicinal Concerns for FDA Approved Diabetes Agents
Kate Petkewicz, PharmD, BCACP, CDE

3:15PM
Break

3:30PM
Basal Insulin: Initiation of Insulin and Advanced Management
Jennifer Rosselli, PharmD, BCPS, BCACP

4:30PM
Advancements in Technology and Incorporation of Self-Management Skills for Patients with Diabetes
Sneha Baxi Srivastava, PharmD, BCACP, CDE
Lalita Prasad-Reddy, PharmD, MS, BCPS, BCACP, CDE

5:30PM
Diabetes Medical Nutrition Therapy: The Role of the Pharmacist
Ms. Anne Daly, MS, RDN, BC-ADM, CDE

Advanced Clinical Management in Diabetes Care

Faculty

Jessica L. Kerr, PharmD, CDE

Dr. Jessica Kerr is an Associate Professor and Assistant Chair for the Department of Pharmacy Practice at Southern Illinois University Edwardsville School of Pharmacy. She received her Bachelor of Science in Pharmacy and Doctor of Pharmacy Degrees from St. Louis College of Pharmacy. Her current practice with within the Belleville Community Based Outpatient Clinic associated with the St. Louis Veterans Affairs Medical Center. She has been a Certified Diabetes Educator since 2004.

Shelley Monroe & Jordan Sinclair, PharmD Candidates

Both Mrs. Monroe and Mr. Sinclair are PharmD Candidate at Southern Illinois University Edwardsville School of Pharmacy. They are currently completing their last experiential year with navigating the pharmacy world to determine where they would like to practice in the future. Both students were instrumental in the development of the Obesity presentation discussed today.

Kate Petkewicz, PharmD, BCACP, CDE

Dr. Kate Petkewicz currently practices as a clinical pharmacy specialist and certified diabetic educator at a community based outpatient clinic that is affiliated with Edward Hines Jr VA. Dr. Petkewicz is privileged to practice as what the VA recognizes as a mid-level practitioner and practices under an independent scope of practice that includes prescribing privileges. Dr. Petkewicz is part of a patient aligned centered team that serves veterans to provide comprehensive medical care.

Jennifer Rosselli, PharmD, BCPS, BCACP

Dr. Jennifer Rosselli is a Clinical Associate Professor at Southern Illinois University Edwardsville School of Pharmacy. She received her Bachelor of Science in Pharmacy and Doctor of Pharmacy degrees from St. Louis College of Pharmacy. She practiced in community pharmacy for several years before completing a pharmacy practice residency through St. Elizabeth's Hospital in Belleville, Illinois. She currently provides clinical pharmacy services for Southern Illinois Healthcare Foundation, a Federally Qualified Health Center network, at the Belleville Family and West Belleville Health Centers where her focus is outpatient diabetes management and cardiovascular risk reduction.

Advanced Clinical Management in Diabetes Care

Faculty

Sneha Baxi Srivastava, PharmD, BCACP, CDE

Dr. Sneha Baxi Srivastava is an Associate Clinical Professor of Pharmacy Practice at Chicago State University College of Pharmacy (CSU-COP) and a clinical ambulatory care pharmacist at ACCESS Community Health Network. Dr. Srivastava received her Doctor of Pharmacy degree in 2004 from the Ernest Mario School of Pharmacy at Rutgers University. Dr. Srivastava clinical interests include self-care, being part of interdisciplinary healthcare team to work with patients with chronic conditions, including diabetes, hypertension, and hyperlipidemia, and medication adherence/patient education. Her research interests include ways to measure and impact medication adherence, the role of psychology in patient's health-related decision making, mindfulness and the impact of various teaching methods on student learning.

Lalita Prasad-Reddy, PharmD, MS, BCPS, BCACP, CDE

Dr. Prasad is a Clinical Assistant Professor of Pharmacy Practice at Chicago State University College of Pharmacy. Dr. Prasad-Reddy received her PharmD degree from Creighton University, in Omaha Nebraska, in 2006, and her Masters in Health Communication (with an emphasis in public health) from Boston University. Dr. Prasad's clinical interests include disease state management, cardiovascular risk reduction, endocrinology, women's health, health communication and outreach, and patient adherence. She is actively involved in global pharmacy initiatives, and most recently traveled to Peru and China on pharmacy mission trips.

Anne Daly, MS, RDN, BC-ADM, CDE

Ms. Daly is a registered dietitian, certified diabetes educator, author, consultant and nationally recognized expert in diabetes care and education, obesity and weight management. Anne is board certified in advanced diabetes management and is a national Past-President, Health Care & Education of the American Diabetes Association. She currently serves as Director of Nutrition & Diabetes Education at Southern Illinois University School of Medicine, Department of Family & Community Medicine. Anne manages a comprehensive diabetes self-management training and support program and provides medical education to faculty and primary care residents. Formerly, she was a co-founder of the Springfield Diabetes & Endocrine Center in Springfield, IL, where she served for 25 years, managing an American Diabetes Association Education Recognized Program and a comprehensive weight management/lifestyle change program. Prior to co-founding the Springfield Diabetes & Endocrine Center with Norman Soler MD.

IPhA Annual Conference
Pre-conference Symposium
September 29, 2016

Advanced Clinical Management in Diabetes Care

THE ROLE OF OBESITY AGENTS FOR WELLNESS

Jessica L. Kerr, PharmD, CDE
Shelley Monroe and Jordan Sinclair, PharmD Candidates
Southern Illinois University Edwardsville School of Pharmacy

Disclosure and Conflict of Interest

- Dr. Jessica L. Kerr
  - In the past has received several community grants from Novo Nordisk in the diabetes arena
  - All honorariums were paid by outside third party
- PharmD Candidates, Shelley Monroe and Jordan Sinclair
  - No disclosures or conflict of issue to report

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Objectives

- Discuss the social and financial impact of obesity in the United States.
- Examine clinical recommendations for screening and treating patients who are overweight.
- Discuss evidence-based medicinal approaches for weight loss in pre-diabetes and diabetes.
- Select and recommend appropriate medication therapy for obesity based on available data.

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Meet Chad…

Chad is a 35 year old male presenting to clinic for routine follow-up.

PMH: T2DM x 5 years, uncontrolled hypertension, hyperlipidemia, hyperthyroidism

Vitals
- BP: 148/92
- HR: 98
- Height: 5'10"
- Weight: 220 lbs.
- Waist circumference: 45 in
- BMI: 31.6 kg/m^2

Current Medications
- Metformin 1000 mg by mouth twice daily
- Albiglutide 50 mg by SQ injection daily
- Amlodipine 5 mg by mouth twice daily
- Metoprolol succinate 100 mg by mouth daily
- Atorvastatin 80 mg by mouth daily

- Allergies: lisinopril (angioedema), losartan (hyperkalemia)

- Labs:
  - CMP – normal except SCr: 1.52 mg/dl
    - CrCl: 59 ml/min
  - A1c: 7.5%

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Question 1

According to the AHA/ACC/TOS guidelines, which risk stratification category does Chad fall into, based on his BMI?

A. Overweight
B. Class I Obesity
C. Class II Obesity
D. Class III Obesity

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Question 2

According the specifics of Chad's case, which of the following agents would be the most appropriate therapy for Chad to trial in weight management?

A. Phentermine/topiramate (Qsymia®)
B. Liraglutide (Victoza®)
C. Naltrexone/bupropion (Contrave®)
D. Lorcaserin (Belviq®)

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Question 3

What type of monitoring should be done by you, the clinician, and at what interval?

A. Educate Chad to decrease his calories to < 800kcals/day, take the medication as prescribed and follow up in 6 months for a 20% weight loss.

B. Educate Chad to follow-up in one year, no monitoring required.

C. Educate Chad to follow-up in 3 months with a goal weight loss of ≥ 11 pounds, evaluate his weight, BMI, waist circumference, and side effects from the medication.

D. Add rapid acting insulin QID, continue all medications and call him in 3 months to get A1c and BMI evaluated then can decide about starting the patient on dual agents for weight loss.

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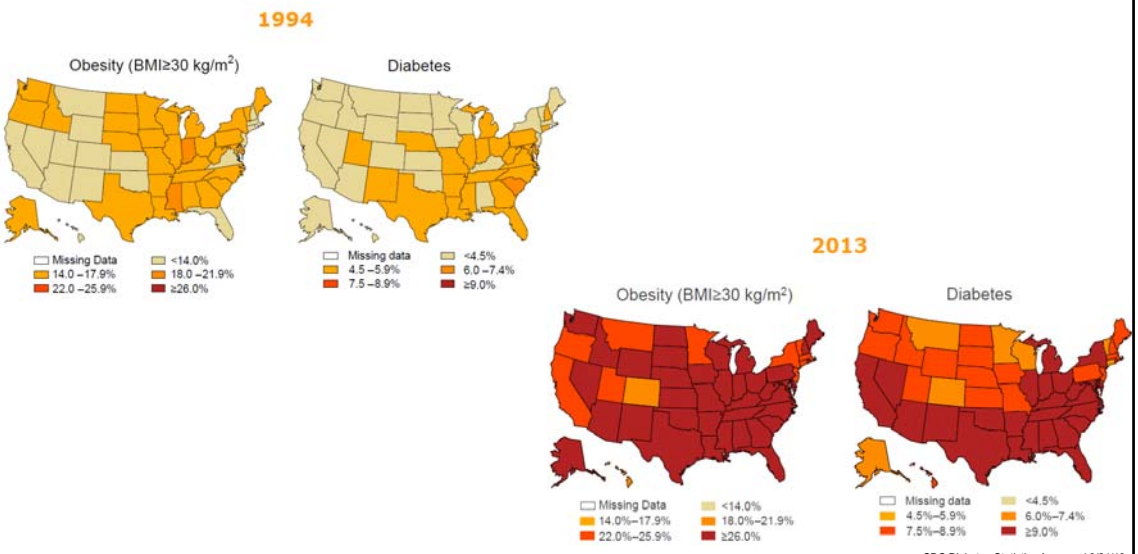
Shear Numbers



CDC Diabetes Statistics Accessed 3/24/16

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Available Clinical Obesity Guidelines

Group	Release Date	Document Name
AHA/ACC/TOS	2013	Guideline for the Management of Overweight and Obesity in Adults
AACE/ACE	2016	Clinical Practice Guidelines for Comprehensive Medical Care of Patients with Obesity
ADA	2016	Standards of Medical Care in Diabetes, 2016 – Obesity Management for Treatment of Type 2 Diabetes

- AHA: American Heart Association
- ACC: American College of Cardiology
- TOS: The Obesity Society
- AACE: American Association of Clinical Endocrinologists
- ACE: American College of Endocrinology
- ADA: American Diabetes Association

J Am Coll Cardiol. 2014 Jul 1: 63(25 Pt B):3029-3030
Endocr Pract. 2016 May 24. [Epub ahead of print]
Diabetes Care 2016 Jan; 39 (Supplement 1): S47-S51

Guideline Recommendations

Guideline	AHA/ACC/TOS	AACE/ACE	ADA
Screening (Height, weight, and BMI)	Annually or more frequently	Annually	Each patient encounter
Waist Circumference (BMI < 35 kg/m^2, increased risk:)	Women: > 88 cm or > 35 in Men: > 102 cm or > 40 in		No recommendation
Risk Stratification (BMI [kg/m^2])	Overweight: > 25-29.9 Class I Obese: 30 to < 35 Class II Obese: 35 to Class III Obese (Extreme Obesity): ≥ 40		Overweight: 25-29.9 Obese: ≥ 30-34.9 Extreme obesity: ≥ 40
Weight Loss	5-10% baseline weight reduction within 6 months	Prevention of diabetes: 10% (other recommendation based on comorbid disease states)	5% reduction for overweight & obese patients with T2DM
Pharmacotherapy (BMI [kg/m^2])	BMI ≥30 or BMI ≥27 + obesity-associated comorbidity*	BMI ≥27	
Bariatric Surgery (BMI [kg/m^2])	BMI ≥40 w/out comorbidity BMI ≥35 + obesity-associated comorbidity	BMI ≥40 w/out complication BMI ≥35 + severe complication BMI 30-34.9 (consideration)	BMI > 35 and T2DM

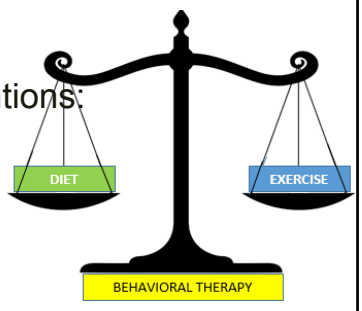
BMI = Body Mass Index (kg/m^2) WC = Waist Circumference T2DM = type 2 diabetes mellitus
*Comorbidities: hypertension, hyperlipidemia, prediabetes, or diabetes

J Am Coll Cardiol. 2014 Jul 1: 63(25 Pt B):3029-3030
Endocr Pract. 2016 May 24. [Epub ahead of print]
Diabetes Care 2016 Jan; 39 (Supplement 1): S47-S51

TREATMENT STRATEGIES

Lifestyle Modifications

High-intensity comprehensive weight loss interventions:



- **Moderately-reduced calorie diet**
  - An energy deficit of ≥500 kcal/day
    - Women: 1,200 - 1,500 kcal/day
    - Men: 1,500 to 1,800 kcal/day
- **Increased physical activity**
  - Aerobic physical activity (brisk walking) for >150 minutes/week
  - No more than 90 minutes at a time of inactivity
- **Behavioral therapy**
  - Focus on adherence programs

J Am Coll Cardiol. 2014 Jul 1: 63(25 Pt B):3029-3030
Diabetes Care 2016 Jan; 39 (Supplement 1): S23-S35

Noradrenergic Agonists

- Diethylpropion CIV (Tenuate®, Tenuate Dospan®)
- Phendimetrazine CIII (Bontril PDM®)
- Benzphetamine CIII (Didrex®, Regimex®)
- Phentermine CIV (Adipex-P®, Suprenza®)
  - Discussed later

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Noradrenergic Agonists

- FDA Indication
  - Short-term (< 12 weeks) adjunct in a regimen of weight reduction based on caloric restriction
    - Diethylpropion and benzphetamine: BMI ≥ 30 kg/m^2
    - Phendimetrazine: BMI ≥ 30 kg/m^2 or ≥ 27 kg/m^2 with risk factors
  - Who have not responded to appropriate weight reducing regimen (diet and/or exercise) alone
- Dosing
  - Diethylpropion
    - IR: 25 mg by mouth three times daily one hour before meals
    - ER: 75 mg by mouth once mid-morning
  - Phendimetrazine
    - 105 mg by mouth once daily 30-60 minutes before morning meal
  - Benzphetamine
    - 25-50 mg by mouth in the morning, may increase to three times daily
- Renal dosing
  - No data, caution in patients with renal impairment

*IR/ER: immediate/extended-release

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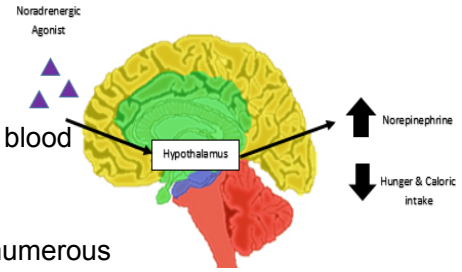
Diethylpropion. Aventis Pharmaceuticals, Inc.; 2003
Phendimetrazine. Epic Pharma, LLC; 2011
Benzphetamine. Pfizer; 2009
Accessed 6/02/2016

Noradrenergic Agonists

- MOA: sympathomimetic amine, similar to amphetamines. Weight reduction likely mediated by the release of catecholamine (norepinephrine) in the hypothalamus resulting in decreased appetite and food intake, but other metabolic effects may also be involved.
- Absorption*
  - Rapid uptake from gastrointestinal tract
- Distribution*
  - Varying lipid-solubility, believed to cross the blood brain barrier and placenta
- Metabolism*
  - Extensive N-dealkylation and reduction → numerous active metabolites
- Elimination*
  - 75-106% of the dose is recovered in the urine within 48 hours after dosing



*Pharmacokinetic data for Diethylpropion (Tenuate®)

Osymia. Vivus, Inc.; 2014
Diethylpropion. Aventis Pharmaceuticals, Inc.; 2003

Noradrenergic Agonists

- Adverse Effects
  - Increased blood pressure, palpitations, urticaria, constipation, nausea, xerostomia, unpleasant taste, dizziness, insomnia, tremor, restlessness, or changes in libido
- Contraindications
  - Pregnancy (category X*) or breastfeeding, cardiovascular disease, glaucoma, hyperthyroidism, agitated state, drug abuse, glaucoma, hypersensitivity to sympathomimetic amines, arteriosclerosis
- Drug Interactions
  - Monoamine oxidase inhibitors (during or within 14 days of use) and tricyclic antidepressants
  - Antihypertensive agents
  - Concomitant use of other “anorectics” or central nervous system stimulants
- Monitoring
  - Weight loss, cardiac/ECHO evaluation for pre-existing/post-treatment development of complications

*Category X: benzphetamine and phendimetrazine
Category B: diethylpropion

Diethylpropion. Aventis Pharmaceuticals, Inc.; 2003
Phendimetrazine. Epic Pharma, LLC; 2011
Benzphetamine. Pfizer; 2009. Accessed 6/02/16

A comparative study of five centrally acting drugs on the pharmacological treatment of obesity

H Suplicy, CL Boguszewski, CMC dos Santos, M do Desterro de Figueiredo, DR Cunha and R Radominski 2014

Drug	n	Weight loss Δ from Baseline
Placebo	29	-3.1 ± 4.3 kg
Diethylpropion (Tenuate®)[a]	28	-10.0 ± 6.4 kg; P<0.001
Sibutramine (Meridia®)[a,b]	30	-9.5 ± 5.9 kg; P<0.001
Mazindol (Mazandor®)[a,b]	29	-7.4 ± 4.9 kg; P<0.01
Fluoxetine (Prozac®)[c]	29	-2.5 ± 4.1 kg
Fenproporex[d]	29	-7.8 ± 6.9 kg; P<0.01

a. FDA indicated for weight loss
b. Removed from the market
c. FDA indicated for depression
d. Not available in the U.S.

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Int J Obes (Lond). 2014 Aug;38(8):1097-103

Phentermine CIV

Adipex-P®, Suprenza®

- Dosing
  - Adipex-P
    - 37.5 mg by mouth daily, administered before breakfast or 1-2 hours after
  - Suprenza
    - 15 mg/30 mg/37.5 mg ODT in the morning with or without food
- Renal Dosing
  - No studies have been completed, caution in patients with renal impairment

ODT = Orally disintegrating tablet

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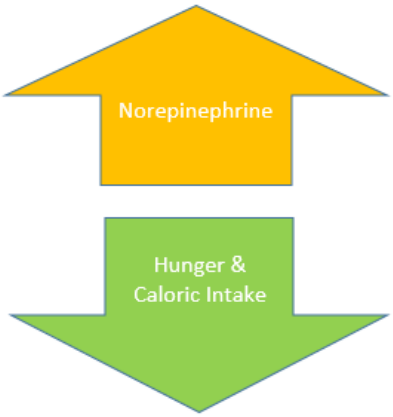
Suprenza (phentermine hydrochloride) ODT. Akrimax Pharmaceuticals, LLC; 2011.
Adipex-P (phentermine hydrochloride USP) for oral use. Teva Pharmaceuticals USA; 2012.

Phentermine

- MOA: sympathomimetic amine, similar to amphetamir
- Absorption
  - Rate and extent similar across formulations
  - ODT formulation absorption decreased:
    - ~5% when taken with a high-fat/calorie meal
    - ~7% if swallowed without prior disintegration
- Distribution
  - 17.5% protein bound
- Metabolism
  - Hepatic via hydroxylation and N-oxidation
  - CYP3A4 substrate (not extensively metabolized)
- Elimination
  - Primarily in the urine (62-85% unchanged)



ODT = Orally disintegrating tablet

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Adipex-P (phentermine hydrochloride USP) for oral use. Teva Pharmaceuticals USA; 2012.

Phentermine

- Adverse Effects
  - Cardiovascular (pulmonary hypertension, valvular disease, ischemic events, increased blood pressure), dizziness, insomnia, euphoria, gastrointestinal upset, erectile dysfunction or changes in libido
- Contraindications
  - pregnancy (category X) and breastfeeding, cardiovascular disease, hyperthyroidism, glaucoma, agitate states, drug abuse, hypersensitivity to sympathomimetic amines
- Drug Interactions
  - Monoamine oxidase inhibitors (during or within 14 days of use)
  - Alcohol use
  - Adrenergic neuron blocking drugs
  - Insulin
- Monitoring
  - Renal function

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Adipex-P (phentermine hydrochloride USP) for oral use. Teva Pharmaceuticals USA; 2012.

Weight Loss of Phentermine vs. Placebo

Kang 2010

Δ from Baseline					
Weight (kg)			WC (cm)		
Phentermine n = 37	Placebo n = 37		Phentermine n = 37	Placebo n = 37	
−8.1 ± 3.9	−1. 7 ± 2. 9	p < 0.001	7.2 ± 0.5	2.1 ± 0.6	p < 0.001

Aronne 2013

	Placebo n = 103	Phentermine 7.5 mg n = 104	Phentermine 15 mg n = 106	Topiramate ER 46 mg n = 102	Topiramate ER 92 mg n = 105	Phen/Top ER 7.5 mg/46 mg n = 103	Phen/Top ER 15 mg/92 mg n = 103
≥ 5% weight loss, n (%)	16 (15.5)	45 (43.3)	49 (46.2)	40 (39.2)	51 (48.6)	64 (62.1)	68 (66.0)
≥ 10% weight loss, n (%)	7 (6.8)	13 (12.5)	22 (20.8)	19 (18.6)	25 (23.8)	40 (38.8)	42 (40.8)
			Δ from Baseline				
Waist circumference, cm (SE)	-3.3 (0.72)	-6.4 (0.72)	-6.6 (0.71)	-5.4 (0.72)	-6.2 (0.72)	-8.8 (0.73)	-8.7 (0.72)

WC = waist circumference
1 inch = 2.54 cm

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Diabetes Obes Metab. 2010 Oct;12(10):876-82.
Obesity (Silver Spring). 2013 Nov;21(11):2163-71.

Phentermine/topiramate extended-release CIV (Qsymia®)

- FDA Indication
  - Adjunct to a reduced-calorie diet and increased physical exercise for chronic weight management in adults with BMI of:
    - ≥ 30 kg/m^2 or ≥ 27 kg/m^2 with ≥ one weight related comorbidity
- Dosing
  - Titration schedule
- Renal dosing
  - CrCl < 30 mL/min, do not exceed 7.5 mg/46 mg once daily dosing
- Hepatic Impairment
  - Child-Pugh score 7 – 9, do not exceed 7.5 mg/46 mg once daily dosing

CrCl = Creatinine clearance

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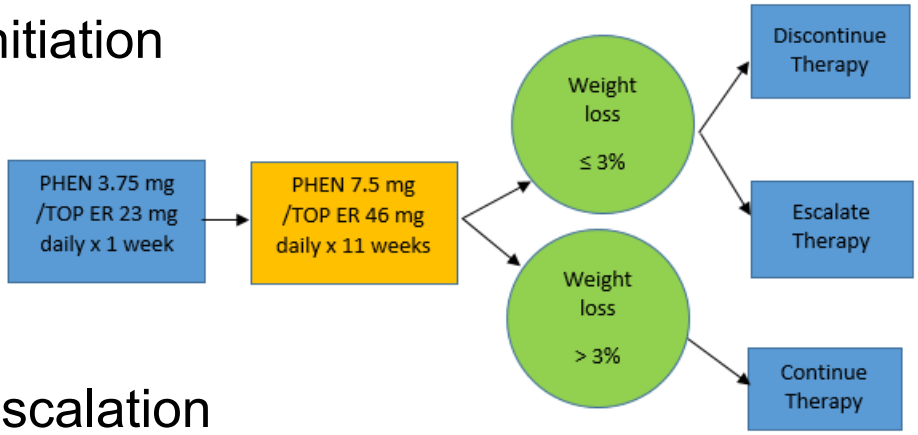
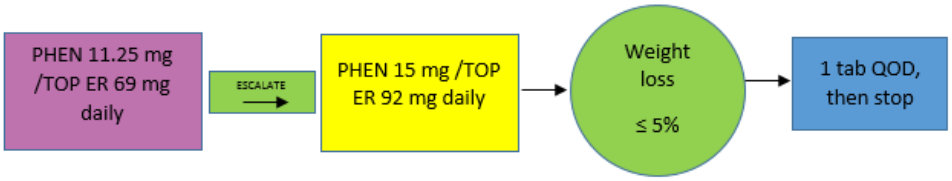
Qsymia. Vivus, Inc.; 2014

Initiation



Escalation



ER = extended-release QOD = every other day

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Phentermine/topiramate extended-release (Qsymia®)

Topiramate ER

- MOA: suppression of appetite and enhanced satiety via:
  - Augmentation of gamma-Aminobutyric acid (GABA) activity
  - Inhibition of excitatory glutamate receptors
  - Carbonic anhydrase inhibition
  - Modulation of voltage-gated ion channels
- Absorption
  - Not affected when taken with a high-fat meal
- Distribution
  - 15-41% plasma protein bound
- Metabolism
  - Not extensively metabolized
- Excretion
  - ~70% unchanged in urine

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Diabetes Metab Syndr Obes. 2013; 6: 131–139.
Qsymia. Vivus, Inc.; 2014
Qsymia ® (phentermine and topiramate). Retrieved from www.Qsymia.com.

Phentermine/topiramate extended-release (Qsymia®)

- Adverse Effects
  - Fetal toxicity, heart rate elevation, suicidal ideation/behavior, acute closed-angle glaucoma, mood and sleep disorders, cognitive impairment, metabolic acidosis
- Contraindications
  - Pregnancy (category X) and breastfeeding, glaucoma, hyperthyroidism, hypersensitivity to other sympathomimetic amines
- Drug Interactions
  - Monoamine oxidase inhibitors
  - Central nervous system depressants (benzodiazepines, barbiturates, sleep agents)
  - Non-potassium sparing diuretics
  - Concurrent administration with:
    - Other carbonic anhydrase inhibitors or antiepileptics
- Monitoring
  - Baseline and periodic chemistry panel that includes bicarbonate, creatinine, potassium, and glucose

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Qsymia. Vivus, Inc.; 2014

EQUIP, CONQUER, and SEQUEL Trials

Efficacy and Safety of Phentermine/topiramate Extended-Release

			PLACEBO		PHEN/TPM 3.75 mg/23 mg		PHEN/TPM 7.5 mg /46 mg		PHEN/TPM 15 mg/92 mg	
STUDY	BMI	DURATION	n	LS Mean Change (%)	n	LS Mean Change (%)	n	LS Mean Change (%)	n	LS Mean Change (%)
EQUIP* Allison 2012	≥ 35	56 weeks	496	-1.55 (0.8 to -2.3)	234	-5.10 (-4.0 to -6.2)			498	-10.92 (-10.2 to -11.7)
CONQUER* Gadde 2011	27 - 45	56 weeks	979	-1.2 (-0.7 to -1.8)			488	-7.8 (-7.1 to -8.5)	981	-9.8 (-9.3 to -10.4)
SEQUEL* Garvey 2012	27 - 45	106 weeks (extension to CONQUER)	196	-2.2 (-1.0 to -3.3)			125	-9.3 (-7.8 to 10.7)	240	-10.7 (-9.7 to 11.8)

*95% CI, *P*-value < 0.001 (vs. placebo)

Progression to T2DM in Patients without Diabetes at baseline

Annualized Incidence Rate (%)

	Placebo	PHEN/TPM 7.5 mg /46 mg	PHEN/TPM 15 mg/92 mg
CONQUER	4.5	3.1	1.9*
SEQUEL	3.7	1.7	0.9**

*RR: 0.47 (0.25–0.88)

**P*-value = 0.0078

26

Obesity (Silver Spring, Md). 2012;20(2):330-342.
Lancet. 2011 Apr 16;377(9774):1341-52.
Am J Clin Nutr. 2012 Feb;95(2):297-308.

Lorcaserin (Belviq®)

- FDA Indication
  - Chronic weight management, as an adjunct to a reduced-calorie diet and increased physical activity in patients with:
  - BMI ≥ 30 kg/m^2 or ≥ 27 kg/m^2 with ≥ one weight related comorbidity (Hypertension, Type 2 Diabetes Mellitus, or Hyperlipidemia)
- Dosing
  - 10 mg by mouth twice daily
  - If ≥5% of body weight has not been lost after 12 weeks, discontinue
- Renal dosing
  - No renal dosing, use is not recommended if CrCl <30 ml/minute or in end stage renal disease

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Lorcaserin. Arena Pharmaceuticals; 2012.

Lorcaserin (Belviq®)

- MOA:
  - Lorcaserin is a selective serotonin 2C (5-HT(2C)) receptor agonist. The exact mechanism of action is not known, but lorcaserin is believed to promote satiety and decrease food intake by activating 5-HT(2C) receptors on anorexigenic pro-opiomelanocortin neurons in the hypothalamus
- Absorption
  - Not affected by food consumption
- Distribution
  - 70% plasma protein bound
- Metabolism
  - Liver: Extensive, two inactive metabolites
- Excretion
  - 92% urine (as metabolites), 2% in feces
  - Half-life: 11 hours

+ Satiety
- Food Consumption

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Lorcaserin. Arena Pharmaceuticals; 2012.

Lorcaserin (Belviq®)

- Adverse Effects
  - Headache, hypoglycemia, nausea, back pain, dizziness, fatigue, dry mouth
- Contraindications
  - Pregnancy
- Drug Interactions
  - Serotonin modulating agents (serotonin syndrome risk)
  - CI with thioridazine (increased plasma levels of thioridazine)
  - Increased risk of hypoglycemia with hypoglycemic agents
- Monitoring
  - Serotonin syndrome, psychiatric/mood changes, blood glucose, priapism

29

Lorcaserin. Arena Pharmaceuticals; 2012.

BLOOM Trial

End Point	ITT Analysis with LOCF Imputation		
Coprimary Endpoints	Lorcaserin (N=1538)	Placebo (N=1499)	P Value
Loss of ≥5% of body weight			
Patients (%)	47.5	20.3	<0.001
Weight Change (kg)	-5.8 +/- 0.2	-2.2+/-0.1	<0.001
Loss of ≥10% of body weight	22.6	7.7	<0.001

ITT= Intention to Treat
LOCF= Last Observed Carried Forward

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N Engl J Med 2010; 363:24
J Clin Endocrinol Metab 96: 3067–3077, 20115-256

BLOSSOM Trial

Lorcaserin Weight Loss					
				P value vs. Placebo	
End Point	Lorcaserin 10 mg BID (N=1561)	Lorcaserin 10 mg daily (N=771)	Placebo (N=1541)	BID	Daily
Patients achieving ≥5% weight loss [N(%)]	737(47.2)	310(40.2)	385(25)	<0.001	<0.001
Patients achieving ≥10% weight loss [N(%)]	353(22.3)	134(17.4)	150(9.7)	<0.001	<0.001
Change in Body Weight (%)	-5.8	-4.7	-2.8	<0.001	<0.001
Baseline Body Weight (kg)	100.3	100.1	100.8		

P value < 0.01 for twice daily vs. daily

31

N Engl J Med 2010; 363:24
J Clin Endocrinol Metab 96: 3067–3077, 20115-256

Naltrexone/bupropion (Contrave®)

- FDA Indication: adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of:
  - ≥ 30 kg/m^2 or ≥ 27 kg/m^2 with ≥ one weight related comorbidity (Hypertension, Type 2 Diabetes, or Hyperlipidemia)
- Dosing: 8 mg naltrexone/90 mg bupropion by mouth according to chart below
- If ≥5% of body weight has not been lost after 12 weeks, discontinue

	Morning Dose	Evening Dose
Week 1	1 tablet	None
Week 2	1 tablet	1 tablet
Week 3	2 tablets	1 tablet
Week 4 – Onward	2 tablets	2 tablets

- Renal dosing
  - No renal dosing, use is not recommended if CrCl <30 ml/minute or in ESRD

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Naltrexone/bupropion ER. Orexigen; 2014.

Naltrexone/bupropion (Contrave®)

- MOA: Naltrexone, an opioid antagonist, and bupropion, a weak dopamine and norepinephrine reuptake inhibitor regulate food intake via effects on the hypothalamus (appetite regulatory center) and the mesolimbic dopamine circuit (reward system). **Not completely understood**
- Absorption
  - Administration with a high-fat meal significantly increases systemic exposure to naltrexone and bupropion (AUC: 2.1-fold and 1.4-fold, respectively) **TAKE ON EMPTY STOMACH**
- Distribution
  - Naltrexone, 21%, and bupropion, 84%, plasma protein bound
- Metabolism
  - Naltrexone: 1 active metabolite
  - Bupropion: 3 active metabolites (all CYP2D6 inhibitors)
- Excretion/Elimination
  - Naltrexone: Half life; 5 hours, 53% to 79% in urine
  - Bupropion: Half-life; 21 hours, 87% in urine, 10% in feces

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Naltrexone/bupropion ER. Orexigen; 2014.

Naltrexone/bupropion (Contrave®)

- Adverse Effects
  - Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, and diarrhea
- Contraindications
  - Uncontrolled hypertension, seizure disorder, chronic opioid use, pregnancy, suicidal ideation/behavior
- Monitoring
  - Renal function, blood pressure, and blood glucose
- Drug Interactions
  - Monoamine oxidase inhibitors
  - Drugs metabolized by and inducers/inhibitors of CYP2D6
  - Medications that lower the seizure threshold
  - Dopaminergic drugs

34

Naltrexone/bupropion ER. Orexigen; 2014.

COR-II Trial

End Point	28 weeks		56 weeks	
	NB32	Placebo	NB32	Placebo
Loss of ≥5% of body weight (%)	55.6	17.5	50.5	17.1
Loss of ≥10% of body weight (%)	27.3	7	28.3	5.7
Baseline Body Weight (kg)	100.3	99.2	100.3	99.2
Change in Body Weight (%)	-6.3	-2	-6.2	-1.3

NB32: Naltrexone/bupropion 32mg/360 mg Baseline BMI, NB32: 36.2, placebo: 36.1 *P* value <0.001 for each endpoint

35

Obesity (Silver Spring). 2013 May; 21(5): 935–943.

COR-BMOD

End Point	56 weeks	
	NB32 + BMOD	Placebo + BMOD
Loss of ≥5% of body weight (%)	66.4	42.5
Loss of ≥10% of body weight (%)	41.5	20.2
Baseline Body Weight (kg)	100.2	101.9
Change in Body Weight (%)	- 9.3	- 5.1

Baseline BMI
NB32 + BMOD: 37.0
Placebo +BMOD: 36.3

NB32: Naltrexone/bupropion 32mg/360 mg
BMOD: Behavioral Modifications

P value <0.001 for each endpoint

36

Obesity (Silver Spring). 2011 Jan; 19(1): 110–120
Obesity (Silver Spring). 2013 May; 21(5): 935–943.

Orlistat (Xenical®,Alli ®)

- FDA Indication
  - Obesity management including weight loss/maintenance when used in conjunction with a reduced-calorie diet.
  - Also indicated to reduce the risk for weight regain after prior weight loss
- Dosing
  - 120 mg by mouth three times daily with each main meal containing fat (Xenical®)
  - 60 mg by mouth three times daily with each main meal contatining fat (Alli®)
  - Meals should be balanced consisting of approximately 30% fat
  - Orlistat should be taken during or up to 1 hour after the meal
- Renal/Hepatic dosing
  - No renal or hepatic dosing due to low systemic absorption

Xenical. Roche Laboratories, Inc. 2015

Orlistat (Xenical®,Alli ®)

- MOA: A reversible inhibitor of gastric and pancreatic lipases, thus inhibiting absorption of dietary fats by 30%.
- Distribution
  - Minimal systemic absorption
- Metabolism
  - Metabolized within the gastrointestinal wall; forms inactive metabolites
- Excretion
  - 97% in feces
  - Half-life: 1 to 2 hours

Xenical. Roche Laboratories, Inc. 2015

Orlistat (Xenical®,Alli ®)

- Adverse Effects
  - Oily spotting, flatus with discharge, fecal urgency, fecal incontinence
- Contraindications
  - Pregnancy, chronic malabsorption syndrome, cholestasis
- Drug Interactions
  - All patients should take a daily multivitamin that includes fat-soluble vitamins (A,D,E,K) and beta-carotene
  - Cyclosporine, Levothyroxine, Warfarin, Amiodarone, Antiepileptic drugs
- Monitoring
  - Body Mass Index, calorie and fat intake, GI intolerance

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Xenical. Roche Laboratories, Inc. 2015

Pooled data from five clinical trials

End Point	1 Year	
	Xenical® N=1072	Placebo N=701
Loss of ≥5% of body weight (%)	57	31
Loss of ≥10% of body weight (%)	20.2	8.1
Change in Body Weight (kg)	-6.1	-2.6

P value <0.001

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Xenical. Roche Laboratories, Inc. 2015

Comparison of Weight Loss Regimens

Agent	Change in weight from baseline (kg)	Metabolism	Cardiac	Pregnancy
Phentermine	-8.1	62-85% urine	Significant ADR	CI
Qsymia (phentermine/topiramate)	-8.0	70% urine	significant ADR	CI
Belviq (lorcaserin)	-5.8	Extensive liver	low risk	CI
Contrave (naltrexone/bupropion)	-6.2	Liver; glucuronidation	mild risk	CI
Xenical (orlistat)	-6.1	No significant	low risk	CI
Saxenda (liraglutide)	-7.9	DPPIV and endopeptidases	mild risk	CI

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REFERENCES: JAMA Intern Med. 2014;174(4):615-619. doi:10.1001/jamainternmed.2013.14629

Glucagon-like peptide-1 receptor agonists

- MOA: Analogs of human glucagon-like peptide-1 (GLP-1) (an incretin hormone) which increases glucose-dependent insulin secretion, decreases inappropriate glucagon secretion, increases B-cell growth/replication, slows gastric emptying, and decreases food intake.
- Injectable therapy
- Weight Reduction: typically 2-3 kg depending on agent
- Safety Concerns: acute pancreatitis, medullary thyroid carcinoma, GI upset
- Place in therapy:
  - One agent FDA approved for weight loss = Saxenda (liraglutide 3 mg), all other GLP1-agonists are only approved for type 2 diabetes
  - 2nd line therapy for type 2 diabetes patients requiring 0.5-1.9% reduction in A1c
  - Patient-specific factors, formulary, cost, and dosing schedule may affect therapy decision

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Diabetes Care 2016 Jan; 39 (Supplement 1): S1-S111
Lexi-Comp Online. 2016

Liraglutide (Saxenda®)

- MOA: Glucagon-like-peptide 1 analog
- Indication:
  - ≥30 kg/m^2 or ≥27 kg/m^2 with hypertension, type 2 diabetes, or hyperlipidemia
- Dosing:
  - Pre-filled, multi-dose pens, can dial up to 0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg or 3 mg
  - Initial dose of 0.6 mg under the skin daily, increasing by 0.6 mg every week until recommended dose of 3 mg is reached.
- Limitations of Use:
  - Not indicated for type 2 diabetes
  - Should not be used with insulin
  - Should not be used with other GLP-1 agonist

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Saxenda. Novo Nordisk. 2016

Liraglutide (Saxenda®)

- Adverse Reactions:
  - Nausea, hypoglycemia, diarrhea, constipation, headache, abdominal pain
- Contraindications:
  - Medullary Thyroid Carcinoma, Multiple Endocrine Neoplasia syndrome, Pregnancy
- Warnings/Precautions:
  - Acute pancreatitis, acute gallbladder disease, heart rate increase
  - Use caution initiating or escalating doses of liraglutide in those with renal impairment

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Saxenda. Novo Nordisk. 2016

Study 1 (Obesity or overweight with comorbidity)

End Point	56 weeks	
	Saxenda® N=2487	Placebo N=1244
Loss of ≥5% of body weight (%)	62.3	34.4
Loss of ≥10% of body weight (%)	33.9	15.4
Baseline Body Weight (kg)	106.2	106.2
Change in Body Weight (%)	-7.4	-3

P values all <0.0001

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Saxenda. Novo Nordisk. 2016

SCALE Trial

End Point	Week 56		
	Liraglutide 3.0 mg (N=412)	Liraglutide 1.8 mg (N=204)	Placebo N=211
Loss of ≥5% of body weight (%)	54.3	40.4	21.4
Loss of ≥10% of body weight (%)	25.2	15.9	6.7
Change in Body Weight (%)	-6	-4.7	-2

P values <0.001 for liraglutide 3.0 mg vs. placebo and 1.8 mg vs. placebo

46

JAMA. 2015;314(7):687-699. doi:10.1001/jama.2015.9676.

Sodium-glucose co-transporter 2 (SGLT2) inhibitors

- MOA: Lowers the renal threshold for glucose and increases urinary glucose excretion by interfering with the reabsorption of renally-filtered glucose across the tubular lumen of the proximal renal tubules
- Oral therapy
- Weight Reduction: 2-3 kg
- Safety Concerns: mycotic genital infection, UTI, dehydration/volume depletion
- Place in therapy:
  - No current FDA indication for weight loss, may motivate patients to change lifestyle
  - 2nd line therapy in type 2 diabetes patients requiring 0.5-1% reduction in A1c
  - Patient-specific factors, formulary, and cost will affect therapy decision

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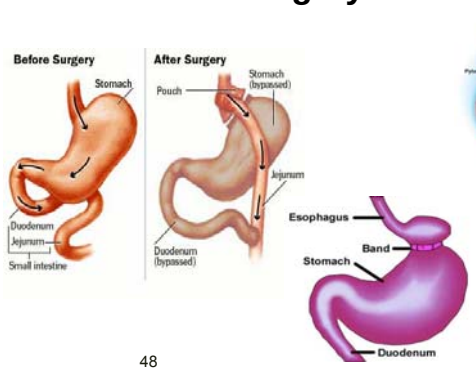
Diabetes Care 2016 Jan; 39 (Supplement 1): S1-S111
Lexi-Comp Online. 2016

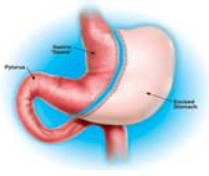
Bariatric Surgery

AHA/ACC/TOS	AACE/ACE	ADA
• BMI ≥40 w/out comorbidity • BMI ≥35 + obesity-associated comorbidity	• BMI ≥40 w/out complication • BMI ≥35 + severe complication • BMI 30-34.9 (consideration)	• BMI > 35 and T2DM

Types of Bariatric Surgery

- Roux-en-Y gastric bypass
- Sleeve gastrectomy
- Gastric band
- Biliopancreatic diversion with duodenal switch gastric bypass





Surg Obes Relat Dis. 2016 Mar-Apr;12(3):468-95

48

Bariatric Surgery

Advantages

- Sjostrom:
  - Normalization of glycaemia 2 years following surgery in 72% of patients
    - As compared with 16% in a matched control group treated with lifestyle and pharmacological interventions
- Schauer:
  - 3 year study in obese patients with uncontrolled type 2 diabetes, A1c targets achieved by:
    - 38% (P < 0.001) in the gastric bypass group
    - 24% (P = 0.01) in the sleeve gastrectomy group
    - 5% in pharmacologically treated group

Disadvantages

- 30-day mortality rates:
  - 0.2% for laparoscopic procedures and 2.1% for open procedures
- Long-term concerns: dumping syndrome (nausea, colic, diarrhea), vitamin and mineral deficiencies, osteoporosis, and, severe hypoglycemia from insulin hypersecretion (rare)

49

JAMA 2014;311:2297–2304
N Engl J Med 2014;370:2002–2013
Surgery 2007;142:621–632
Diabetes Care 2016 Jan; 39 (Supplement 1): S47-S51

Meet Chad…

Chad is a 35 year old male presenting to clinic for routine follow-up.

PMH: T2DM x 5 years, uncontrolled hypertension, hyperlipidemia, hyperthyroidism

Vitals

- BP: 148/92
- HR: 98
- Height: 5'10"
- Weight: 220 lbs.
- Waist circumference: 45 in
- BMI: 31.6 kg/m^2

Current Medications

- Metformin 1000 mg by mouth twice daily
- Albiglutide 50mg by SQ injection daily
- Amlodipine 5mg by mouth twice daily
- Metoprolol succinate 100mg by mouth daily
- Atorvastatin 80mg by mouth daily

- Allergies: Lisinopril (angioedema), Losartan (Hyperkalemia)

- Labs:
  - CMP – normal except SCr: 1.52 mg/dl
    - CrCl: 59 ml/min
  - A1c: 7.5%

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Question 1

According to the AHA/ACC/TOS guidelines, which risk stratification category does Chad fall into, based on his BMI?

A. Overweight
B. Class I Obesity
C. Class II Obesity
D. Class III Obesity

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Question 2

According the specifics of Chad's case, which of the following agents would be the most appropriate therapy for Chad to trial in weight management?

A. Phentermine/topiramate (Qsymia®)
B. Liraglutide (Victoza®)
C. Naltrexone/bupropion (Contrave®)
D. Lorcaserin (Belviq®)

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Question 3

What type of monitoring should be done by you, the clinician, and at what interval?

A. Educate Chad to decrease his calories to < 800kcals/day, take the medication as prescribed and follow up in 6 months for a 20% weight loss.

B. Educate Chad to follow-up in one year, no monitoring required.

C. Educate Chad to follow-up in 3 months with a goal weight loss of ≥ 11 pounds, evaluate his weight, BMI, WC, and side effects from the medication.

D. Add rapid acting insulin QID, continue all medications and call him in 3 months to get A1c and BMI evaluated then can decide about starting the patient on dual agents for weight loss.

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Advanced Clinical Management in Diabetes Care

THE ROLE OF OBESITY AGENTS FOR WELLNESS

Jessica L. Kerr, PharmD, CDE
Shelley Monroe and Jordan Sinclair, PharmD Candidates

IPhA Annual Conference
Pre-conference Symposium
September 29, 2016

Advanced Clinical Management in Diabetes Care

ADVANCED CLINICAL MEDICINAL CONCERNS FOR FDA APPROVED DIABETES AGENTS

Katherine A Petkewicz PharmD, CDE
Edward Hines Jr VA
Clinical Pharmacist, Ambulatory Care

Disclosure and Conflict of Interest

- Dr. Katherine A Petkewicz
  - All honorariums were paid by outside third party.
  - No conflicts of interest to disclose

2

Objectives

- Discuss cardiovascular outcomes with diabetes drug therapies.
- Discuss clinical concerns for metformin, thiazolidinediones, incretin-based therapies, and sodium glucose transport 2 inhibitors.
- Assess patient populations with type 2 diabetes to eliminate possible negative clinical outcomes or contraindications to therapy.
- Describe strategies to educate patients about risks versus benefits to these agents.

3

Meet Mrs. P

PMH: T2DM ,HTN, Dyslipidemia, CKD, CHF, Osteoporosis, considerable h/o hyopglycemia

Age:78 yo

Vitals
- BP: 108/60mmHg
- HR: 68bpm
- Height: 5'2"
- Weight: 110 lbs.

Current Medications

--Glargine 45 units twice daily
--Hydrochlorothiazide 25mg daily
--Lisinopril 10mg daily
--Atorvastatin 40mg by mouth daily
--Alendronate 70mg weekly
--Calcium Carbonate 600mg twice daily
--Cholecalciferol 2000 units daily
--Aspirin 81mg daily

Allergies: NKA
Labs:
** LFTS WNL
** CHEM 7 WNL except:
-SCR 1.62, EGFR 30 ml/min
** A1c: 8.4%

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Question 1

- Which of the following recommendations would not be appropriate at this time?
  - *A. Canagliflozin*
  - *B. Glipizide*
  - *C. Pioglitazone*
  - *D. All of the above*

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Question 2

- Mrs. P refuses further injections. Which of the following would be most appropriate given her PMH?
  - *A. Alogliptin*
  - *B. Saxagliptin*
  - *C. Sitagliptin*
  - *D. None of the above*

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Question 3

- Which of the following are strategies demonstrated to support shared decision making?

A. *Active Listening*
B. *Teach Back Technique*
C. *Deciding to do nothing*
D. *All of the above*

7

Cardiovascular Safety and Diabetes Medications

- Rosiglitazone
- FDA Requirements 2008
  - *Outcome studies for all new diabetes medications*
  - *Primary Outcome/Composite*
    - Major Adverse Cardiovascular Event (MACE)
      - *CV death*
      - *Non-fatal MI*
      - *Non-fatal stroke*
- **ENSURE NEWER AGENTS AT LEAST NEUTRAL OR BENEFICIAL IN REGARD TO CV OUTCOMES**

Menon V, et al. *Circulation*. 2014;129:2705-2713

8

Cardiovascular Aspects with DPP4 inhibitors

Study	Drug	Inclusion Criteria	Results/Conclusions
SAVOR-TIMI 53	Saxagliptin	Established CV or multiple RFS for vascular dx	No significant difference in MACE Increased rate of hospitalizations for HF
EXAMINE	Alogliptin	Acute coronary event within previous 15-90 days	No significant difference in MACE Increased rate of hospitalizations for HF
TECOS	Sitagliptin	Established CV disease	No significant difference in MACE

Scirica et al. *N Engl J Med.2013;369(14)*:1317-1326.
White WB, et al.. *N Engl J Med.*2013;369(14):1327-1335.
Zannad F, et al. *Lancet.*2015;385:2067-2076.

9

Cardiovascular Aspects with GLP-1 analogs

Study	Drug	Inclusion Criteria	Results/Conclusions
ELIXA	Lixisenatide	Acute coronary event within previous 180 days	No significant difference in MACE
LEADER	Liraglutide	HbA1c>7% Age ≥50yo and CV Dx Age ≥60 and ≥1 CV risk factor	• Tx group lower risk of primary outcome • Lower risks of death from CV causes • Lower risk of death from any cause • Lower risk of microvascular events

Pfeffer MA, et al. *N Engl J Med.2015;3733:2247-57*
Marso SP, et al. *N Engl J Med. 2016;375(4):311-322.*

10

Cardiovascular Aspects with SGLT-2 inhibitors

Study	Drug	Inclusion Criteria	Results/Conclusions
EMPA-REG	Empagliflozin	Established CV disease	MACE is lower in empagliflozin

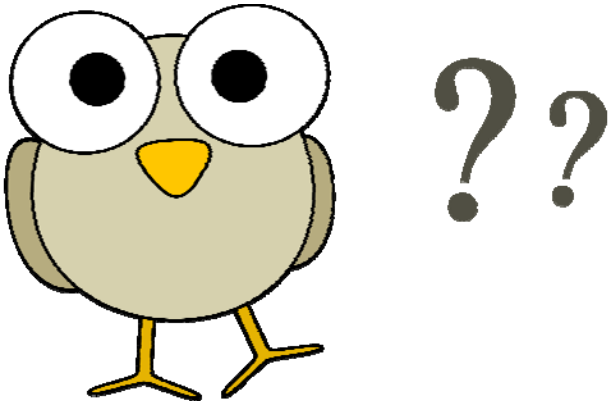
CANVAS TRIAL: **CANagliflozin cardioVascular Assessment Study**
T2DM age > 30 years old with Cardiovascular Disease
Placebo vs. 100mg or 300mg of canagliflozin

OUTCOME: Major adverse cardiovascular events, including CV death, nonfatal myocardial infarction (MI), and nonfatal stroke (April 2017)

DECLAIR TRIAL: **Multicenter Trial to Evaluate the Effect of Dapagliflozin on the Incidence of Cardiovascular Events (DECLARE-TIMI58)**
T2DM age > 40 years at risk for CV Disease
Placebo vs. 10mg of dapagliflozin
OUTCOME: Time to first event included in the composite endpoint of CV death, MI or ischemic stroke (April 2019)

Zinman B, et al. *N Engl J Med* 2015;373:2117-28. 11

WHAT ABOUT MY PATIENT



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Clinical Concerns: Metformin

- Lactic Acidosis
  - *Heart Failure*
  - *Hepatic Disease*
- Chronic Kidney Disease (CKD)/Renal Insufficiency (RI)
- B12 Deficiency

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Clinical Concerns: Metformin

- Lactic Acidosis
  - *Concern may lead to underutilization of metformin*
  - *Salpeter et al*
    - Review of comparative trials and cohort studies upper limit of true incidence of lactic acidosis with metformin 6.3 per 100,000 patient-years
      - *7.8 cases per 100,000 patient years in pt without metformin*
      - *Conclusion: no increase lactic acidosis risk with use of metformin*

Salpeter S, et al. *Cochrane Database Syt Rev 2010;(4):CD002967* 14

Clinical Concerns: Metformin

- Chronic Kidney Disease (CKD) /Renal Insufficiency (RI)
  - Traditional training:
    - Metformin contraindicated in males with SCR ≥1.5
    - Metformin contraindicated in females with SCR ≥1.4
  - *Update:*
    - FDA required label changes
      - *Metformin may be used with mild to moderate kidney impairment*
      - *Treatment decision with metformin to be based on* ***eGFR not SCR***

http://www.fda.gov/Drugs/DrugSafety/ucm493244.htm

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Clinical Concerns: Metformin

eGFR (mL/min/1.73 m²)	FDA Recommended Dose/Action	Frequency of Monitoring Renal Function (or more frequently as warranted)
<45ml/min	If pt on metformin eGFR later falls <45ml/min assess risk vs. benefit	More frequently
30-45ml/min	Do not start metformin	More frequently
<30ml/min	Metformin Contraindicated/Discontinue	N/A

Parameters to Consider with IV contrast	Recommended Action
EGFR 30-60ml/min	Metformin withheld prior to procedure
Patients h/o liver dx, alcoholism, heart failure	Metformin withheld prior to procedure

http://www.fda.gov/Drugs/DrugSafety/ucm493244.htm

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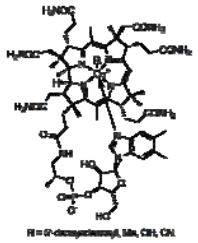
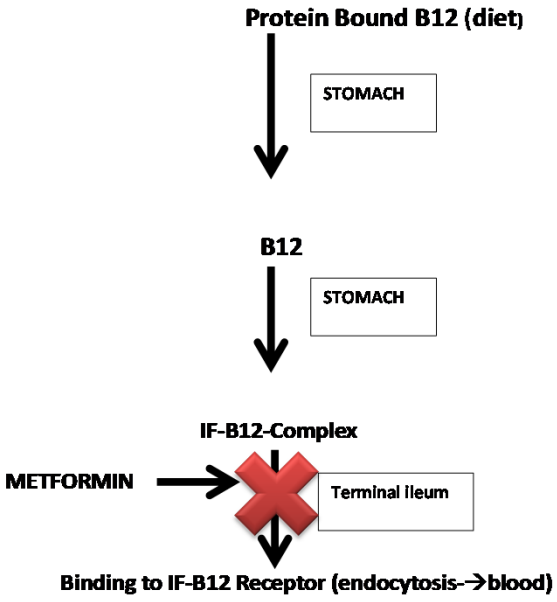
Clinical Concerns: Metformin



- B12 Deficiency
  - *Long term metformin use may lead to B12 deficiency*
  - *14 patients with metformin vs. placebo for 4.3 years leads to one additional diagnosis of B12 deficiency*

De Jager J, et al. *BMJ* 2010;340:C2181.
Aroda VR, et al. *J Clin Endocrinol Metab*, April 2016,101(4):1754-1761.



Clinical Concerns: DPP-4 Inhibitors

- **Heart Failure**
  - *Bottom line evidence remains mixed*
    - Currently if risk exists appears minimal
    - Consider existing cardiovascular disease or risks for vascular disease
      - *Metanaylsis of 5 randomized trials pooled data results:*
        - Borderline increased risk of heart failure related admissions with –DPP4 inhibitors
        - Event rate DPP4inhibitor 3.4% vs 3% controls
          - *(OR 1.13, 95% CI 1.00-1.26)*
          - *Risk difference 8 more admissions per 1000 T2DM patients treated with DPP4i for >5 years*

Li L, et al. *BMJ* 2016;352:i610 19

Clinical Concerns: DPP-4 Inhibitors

- *FDA April 2016*
  - Added new Warnings and Precautions to the labels of medicines that contain saxagliptin or alogliptin to inform of the potential increased risk of heart failure

http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm494252.htm 20

Clinical Concerns: DPP-4 Inhibitors

- **Joint Pain**
  - *FDA drug safety communication 8-28-2015*
- **FDA warns that DPP-4 inhibitors for type 2 diabetes may cause severe joint pain**
  - *"may cause joint pain that can be severe and disabling"*
  - Symptoms from 1 day to years after start of DPP-4 inhibitor.
  - Once DPP-4 inhibitor agent discontinued symptoms resolved quickly
  - Possible recurrence with re-challenge

http://www.fda.gov/Drugs/DrugSafety/ucm459579.htm 21

Clinical Concerns: DPP-4 Inhibitors

- **Acute Pancreatitis**
  - *1 additional case for every 50 patients treated for up to 2 years*
- Consider risks for pancreatitis
  - *Elevated TG*
  - *Gallstones*
  - *Heavy alcohol use*
  - *Tobacco*
  - *Obesity*
  - *Age (>60)*

Whitcomb DC. Clinical practice. Acute pancrea
N Engl J Med 2006;354:2142-50. 22

Clinical Concerns: DPP-4 Inhibitors

- **Pancreatitis**
  - *Agents carry Warning and Precautions labeling*
    - *Unclear if increased risk in patients with h/o pancreatitis*
- Educate patients
  - *Signs/symptoms*
    - Severe abdominal pain, may radiate
    - Nausea
    - Vomiting
- Do not re-challenge
- Suggestive not definitive as of now

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Clinical Concerns: GLP-1 Agonists

- Pancreatitis
  - *Same as previous slides with DPPIV-Inhibitors*
    - Consider other risk factors in your patient
- Medullary Thyroid Carcinoma
  - *Bottom line in humans uncertain/unclear*
  - *Do not use in persons with personal or family history of:*
    - Medullary thyroid carcinoma
    - Multiple endocrine neoplasia syndrome type 2 (MEN 2)

Li L,et al. *BMJ;348:g2366.*
Victoza® [package insert]. Princeton, NJ: Novo Nordisk;2010.

24

Clinical Concerns: SGLT2 inhibitors

- **Amputations**
- CANVAS
  - *Canagliflozin Cardiovascular Assessment Study*
- Patient Education
  - *Monitor for pain, sores or ulcers, infections*

25

Clinical Concerns: SGLT2 inhibitors

- **Bone fractures**
  - *FDA drug safety communication 9-10-2015*
- **FDA revises label of diabetes drug canagliflozin (Invokana, Invokamet) to include updates on bone fracture risk and new information on decreased bone mineral density**
  - At 2 years, patients randomized to canagliflozin 100 mg and canagliflozin 300 mg had placebo-corrected declines in BMD at the total hip of 0.9% and 1.2%, respectively, and at the lumbar spine of 0.3% and 0.7%, respectively. Additionally, placebo-adjusted BMD declines were 0.1% at the femoral neck for both canagliflozin doses and 0.4% at the distal forearm for patients randomized to canagliflozin 300 mg.

FDA. *Invokana* and *Invokamet* (canagliflozin): drug safety communication – new information on bone fracture risk and decreased bone mineral density. September 10, 2015. http://www.fda.gov/safety/medwatch/safetyinformation/safetyalertsforhumanmedicalproducts/ucm461876.htm.

26

Clinical Concerns: SGLT2 inhibitors

- Bone Fractures
- Proposed mechanism
  - *Increased falls secondary to hypotension from diuretic effect of SGLT2 Inhibitors*

FDA. *Invokana* and *Invokamet* (canagliflozin): drug safety communication – new information on bone fracture risk and decreased bone mineral density. September 10, 2015. http://www.fda.gov/safety/medwatch/safetyinformation/safetyalertsforhumanmedicalproducts/ucm461876.htm. 27

Clinical Concerns: SGLT2 inhibitors

- Ketoacidosis
  - *FDA drug safety communication 5-15-2015*
  - SGLT2 inhibitors for diabetes may result in a serious condition of too much acid in the blood
    - *The high anion gap metabolic acidosis accompanied by elevation in urine or serum ketones in the reported cases was **not** associated with the very high glucose levels that are typical for diabetic ketoacidosis.*
    - *Half of cases identified had no identified contributing factor*
    - *Type 1 and Type 2 cases noted*

FDA. SGLT2 inhibitors: drug safety communication – FDA warns medicines may result in a serious condition of too much acid in the blood. May 15, 2015. http://www.fda.gov/safety/medwatch/safetyinformation/safetyalertsforhumanmedicalproducts/ucm446994.htm 28

Clinical Concerns: SGLT2 inhibitors

- Ketoacidosis
- AACE/ACE Position Statement Conclusions
  - *Small number of DKA cases in trials with canagliflozin and empagliflozin*
  - *Patient presentation may be atypical*
  - *Provider education is important*
  - *SGLT2 inhibitor benefits>>>risks*

Endocr Pract.2016;22:753-762. 29

Clinical Concerns: SGLT2 inhibitors

Signs and Symptoms DKA
Polyuria
Polydipsia
Nausea/ Vomiting / Abdominal Pain
Vision
Lethargy
Tachycardia
Kussmaul respirations
Acetone breath

DKA Diagnostic Criteria	
Parameter	Lab Value
Arterial pH	<7.3
Beta Hydroxybutyrate	≥40mg/dl adults
Serum ketone	Positive
Anion gap	>10
Mental status	Drowsy, lethargic, coma

Endocr Pract.2016;22:753-762. 30

Clinical Concerns: SGLT2 inhibitors

- **DKA Prevention**
  - *Stop SGLT2 inhibitors at least 24 hours before surgery or other precipiatory events*
  - *Close monitoring anion gap, arterial pH, serum beta-hydroxybutyrate*
- **Patient Counseling**
  - *Avoid excessive alcohol ingestion*
  - *Avoid ketogenic diets*

Endocr Pract.2016;22:753-762. 31

Clinical Concerns: TZDs

- **Bladder Cancer**
  - *FDA drug safety communication 09-17-2010 (updates 6/15/11 and 8/4/11)*
- **Ongoing Safety Review of Actos (pioglitazone) and Potential Increased Risk of Bladder Cancer After Two Years Exposure**
  - Risk of bladder cancer increased with increasing dose and duration of pioglitazone use
  - Absolute risk remains low

http://www.fda.gov/Drugs/DrugSafety/ucm259150.htm

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Clinical Concerns: TZDs

- **Bone Fractures**
  - *AR Males 1%*
  - *AR Females 3%*

Diabetes Care. 2014:37:2647-2659
Diabetes Care. 2015:38:140-149.

33

Clinical Concerns: TZDs

- **Heart Failure (HF)**
  - *AR for HF requiring hospitalizations small*
  - *No increase in fatal heart failure*

Diabetes Care. 2014:37:2647-2659
Diabetes Care. 2015:38:140-149.

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Discussing Options with Patients

- Set the stage
  - *Patient-focus first*
  - *Practitioner-focus second*
- Shared Decision Making (SDM)
  - *Decision aids/tools*

35

Discussing Options with Patients: SDM

- The Mayo Clinic Shared Decision Making National Resource Center advances patient-centered medical care by promoting shared-decision making through the development, implementation, and assessment of patient decision aids and shared decision making techniques.

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Discussing Options with Patients

- **Medical**
  - A1C→what is desired A1C lowering?
  - Renal and hepatic function and other medical history
  - Concomitant medications
- **Economic**
  - Insurance/co-pays etc…
- **Safety**
  - *Risk versus benefit*

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Discussing Options with Patients

- Ideal agent?
  - *Easy administration*
  - *Unlikely symptomatic side effects leading to nonadherence*
  - *Inexpensive*
  - *Reliably efficacious & safe*

Diabetes Care. 2014:37:2647-2659.

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Class Overview

Class	Efficacy	Advantages	Disadvantages
Biguanides	A1C↓ 1-1.5%	"Old" Inexpensive Weight Neutral - Hypoglycemia ↓CVD events (UKPDS)	GI side effects Renal considerations
Sulfonylureas	A1C↓ 1-2%	"Old" Inexpensive ↓Microvascular risk (UKPDS)	Hypoglycemia ↑ Weight ↓Efficacy over time ↓Durability
Thiazolidinediones	A1C↓ 0.5-1.4%	Inexpensive (pio) - Hypoglycemia ↓CVD events (? pio)	↑ Weight Edema Heart Failure Bone fractures ↑Risk bladder cancer -(pioglitazone)

Diabetes Care. 2014:37:2647-2659
Diabetes Care. 2015:38:140-149.

39

Class	Efficacy	Advantages	Disadvantages
Dipeptidyl peptidase-4 (DPP-4) Inhibitors	A1C↓0.5-0.8%	Weight Neutral -Hypoglycemia Well tolerated	"New" Expensive Acute pancreatitis HF hospitalizations? Derm
Sodium-glucose cotransporter 2 (SGLT2) Inhibitors	A1C↓ 0.5-1.0%	-Hypoglycemia Weight loss (2kg) ↓BP	"New" Expensive GU infection Hypotension ↑LDL
Glucagon-like peptide (GLP-1) Agonists	A1C↓ 0.5-1.0%	-Hypoglycemia Weight loss	"New" Expensive GI (N/V/D) Injectable C-cell hyperplasia/medullary thyroid tumors in animals Pancreatitis
Insulin	A1C ↓ N/A	"Old" Inexpensive	Hypoglycemia Weight Gain Injection SMBG

Diabetes Care. 2014:37:2647-2659
Diabetes Care. 2015:38:140-149.

Discussing Options with Patients

- **Bottom Line**
  - *"Regardless of the specific therapy selected, the overarching goal should be to safely achieve glycemic control at the earliest possible stage with the least risk for adverse events, thereby increasing likelihood of long-term durability of control and avoidance of complications in the future"*

Diabetes Care. 2014:37:2647-2659 41

Meet Mrs. P

PMH: T2DM ,HTN, Dyslipidemia, CKD, CHF, Osteoporosis, considerable h/o hyopglycemia

Age:78 yo

Vitals
- BP: 108/60mmHg
- HR: 68bpm
- Height: 5'2"
- Weight: 110 lbs.

Current Medications

--Glargine 45 units twice daily
--Hydrochlorothiazide 25mg daily
--Lisinopril 10mg daily
--Atorvastatin 40mg by mouth daily
--Alendronate 70mg weekly
--Calcium Carbonate 600mg twice daily
--Cholecalciferol 2000 units daily
--Aspirin 81mg daily

Allergies: NKA
Labs:
** LFTS WNL
** CHEM 7 WNL except:
-SCR 1.62, EGFR 30 ml/min
** A1c: 8.4%

42 42

Question 1

- Which of the following recommendations would not be appropriate at this time?
  - *A. Canagliflozin*
  - *B. Glipizide*
  - *C. Pioglitazone*
  - *D. All of the above*

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Question 2

- Mrs. P refuses further injections. Which of the following would be most appropriate given her PMH?
  - *A. Alogliptin*
  - *B. Saxagliptin*
  - *C. Sitagliptin*
  - *D. None of the above*

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Question 3

- Which of the following are strategies demonstrated to support shared decision making?

  A. *Active Listening*
  B. *Teach Back Technique*
  C. *Deciding to do nothing*
  D. *All of the above*

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IPhA Annual Conference
Pre-conference Symposium
September 29, 2016

Advanced Clinical Management in Diabetes Care

ADVANCED CLINICAL MEDICINAL CONCERNS FOR FDA APPROVED DIABETES AGENTS

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IPhA Annual Conference
Pre-conference Symposium
September 29, 2016

Advanced Clinical Management in Diabetes Care

Basal Insulin: Initiation of Insulin and Advanced Management

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Disclosure and Conflict of Issue

- Jennifer Rosselli reports grant support from Novo Nordisk for community and patient health education.

OBJECTIVES

At the conclusion of this program, the pharmacist will be able to:

- Identify indications for initiating basal insulin in persons with type 2 diabetes.
- Compare and contrast commercially available basal insulin preparations.
- Develop basal insulin regimens, based on patient-specific parameters, that align with current expert guidelines and/or clinical evidence.
- Describe the pharmacist's role in overcoming challenges and barriers to insulin therapy.

Meet KD, a 57-year-old WF.....

- Presenting for DM disease state management at the family medicine clinic. She has a 10-year history of diabetes.
- On metformin 1000 mg po BID since her diagnosis and glipizide was increased to 10 mg po BID 3 months ago.
- She reports monitoring home fasting BG most days with all levels between 250 mg/dL and upwards of 300s.
- She was resistant to the idea of insulin 3 months ago (at 1st Pharm.D. encounter with patient).
- Encounter note from PCM 3 weeks ago indicates insulin was discussed and patient is now ready to start it, initiation deferred to Pharm.D. service.

KD case, continued

- Other medical problems: HTN, asthma, OSA, peripheral neuropathy
- Other medications: atorvastatin 80 mg/day, lisinopril 20 mg po daily, gabapentin 300 mg po TID, albuterol HFA 2 puffs Q 4-6 h
- Ht 5 ft. 8 in., Wt 126 kg, BMI 42.3 kg/m^2
- Vitals

Today	2 months ago
BP 126/80 mmHg, HR 68 bpm	142/80 mmHg, HR 70 bpm

- A1C 10.8% as of 1 week ago, down from 11.3% 3 months ago
- All other labs within normal limits, SCr 0.76 mg/dL

Question 1

Which of the following is an indication for KD to start insulin according to the American Association of Clinical Endocrinologists? SELECT ALL THAT APPLY

a. A1C goal not achieved after 3 months of dual therapy
b. A1C > 7.5% and taking dual noninsulin therapy
c. A1C > 9% regardless of symptoms
d. T2DM diagnosed 10 years ago

Question 2

Which of the following is the most appropriate diabetes therapy change for KD?

a. Initiate basal insulin 0.5 units/kg/day
b. Initiate basal and mealtime insulin (TDD 0.5 units/kg/day, 50% basal and 50 % mealtime)
c. Initiate basal insulin 0.2 units/kg/day
d. Initiate basal 0.2 units/kg/day and increase glipizide to 20 mg po BID

KD returns 6 months later with a Rx for glucagon

- Her A1C has decreased; however, she is having "night sweats" about 4 times per week in the middle of the night
- Has been eating a bedtime snack to try to prevent, but the problem is still occurring
- Reports good adherence, administers at the same time daily
- Her primary care provider has been altering insulin dosages to limit these night time hypoglycemic reactions but has not had success

Medications include:

- Metformin 1000 mg BID x 10 years
- Lantus 60 units at bedtime daily
- Stopped glipizide due to hypoglycemia

Question 3

Which therapy would be an option for KD to gain glucose control and potentially avoid hypoglycemia?

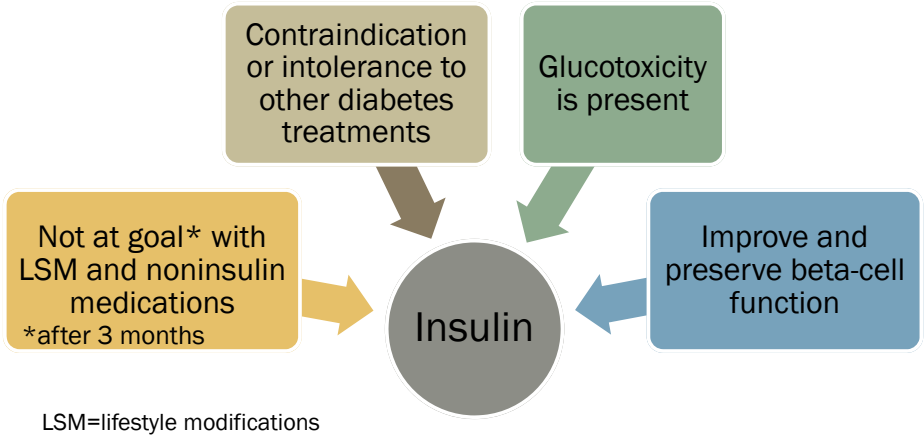
a. Start inhaled insulin at 24 units TID
b. Continue all medications and initiate insulin aspart 70/30 pre-mix
c. Switch glargine U-100 to glargine U-300 or insulin degludec
d. Switch glargine U-100 to "follow on" glargine U-100

Background

- Despite numerous treatment options, 30% to 50% of adults with diabetes fail to meet their glycemic goals
- Clinical guidelines endorse initiating basal insulin as a first- or second-line type 2 diabetes treatment
- Fewer than one-third of patients treated with basal insulin obtain a hemoglobin A1C < 7%
- Many barriers to insulin use and potential adverse effects are largely responsible for its underutilization

Ali, et al. N Engl J Med 2013;368:1613-24.
Cutis B, et al. J Med Econ 2014;17:21-31.

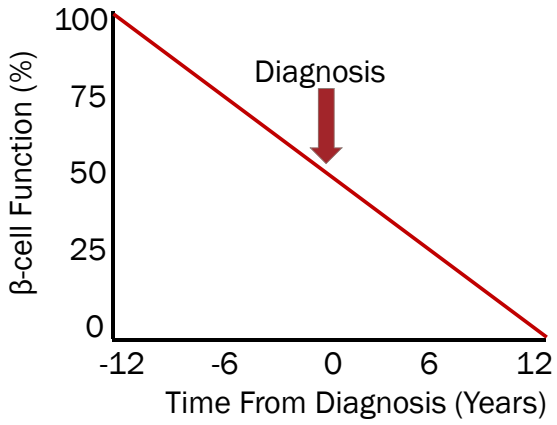
When to Consider Initiation of Insulin in Type 2 Diabetes



LSM=lifestyle modifications
(healthy eating, weight control, increased physical activity)

Inzucchi et al. Diabetes Care 2012;35:1364-1379.

β-Cell Function in Type 2 Diabetes



U.K. Prospective Diabetes Study Group. Diabetes 1995;44:1249-58.

Comparison of Guideline Recommendations for Initiating Insulin

ADA	AACE / ACE

• A1C goal not achieved after 3 months of noninsulin mono- or dual therapy
• At diagnosis with overt symptoms and/or severe hyperglycemia (A1C ≥ 9%)
  • With or without additional medications
	• A1C goal not achieved after 3 months of noninsulin mono- or dual therapy
	• A1C ≥ 7.5% as dual therapy option
	• A1C > 9% and symptomatic
	  • With or without additional medications

ADA=American Diabetes Association

ACE=American College of Endocrinology
AACE=American Association of Clinical Endocrinologists

Diabetes Care 2016;39(Suppl. 1.
Endocr Pract. 2016;22:84-113

ADA Recommendations for Initiating and Adjusting Basal Insulin

Initiate
- Usually with metformin ± other noninsulin medication
- 10 units/day or 0.1 – 0.2 units/kg/day

Titrate
- Once or twice weekly to reach targeted fasting blood glucose (FBG)
- Increase dose by 10 – 15% or by 2 – 4 units

If HypoG
- Identify and address causes of hypoglycemia
- Decrease dose by 4 units or 10 – 20%

HypoG=hypoglycemia

Diabetes Care 2016;39(Suppl. 1.

AACE / ACE Recommendations for Initiating and Adjusting Basal Insulin

Titrate every 2 to 3 days to reach targeted glycemic goals

- ❖ Fixed regimen: increase total daily dose (TDD) by 2 units
- ❖ Adjustable regimen:
  - FBG > 180 mg/dL: add 20% of TDD
  - FBG 140-180 mg/dL: add 10% of TDD
  - FBG 110-139 mg/dL: add 1 unit
- ❖ If hypoglycemia, reduce TDD by:
  - BG < 70 mg/dL: 10%-20%
  - BG < 40 mg/dL: 20%-40%

FBG=fasting blood glucose, BG=blood glucose, SFU=sulfonylurea

Endocr Pract. 2016;22:84-113

Why are so few patients reaching their glycemic goals with insulin?

Benefits and Barriers of Insulin Therapy

Benefits

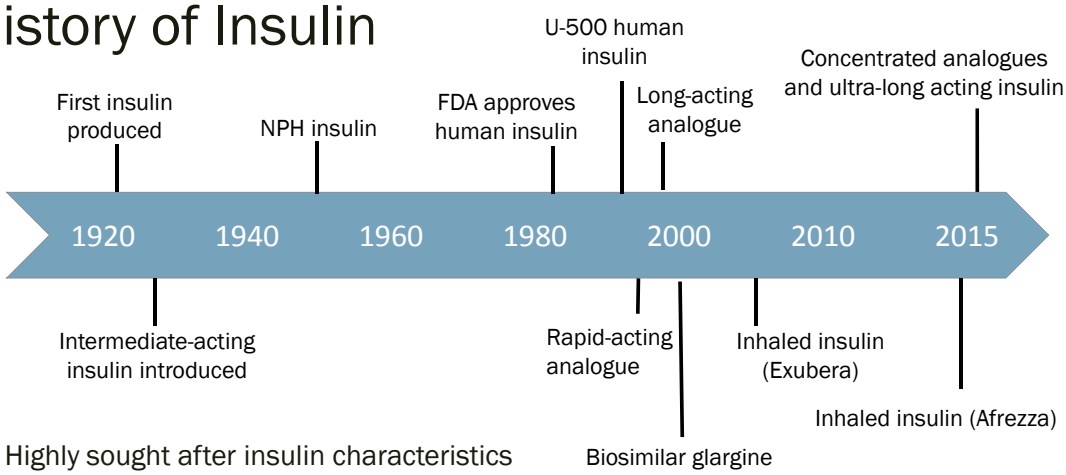
- All patients should respond
- Unlimited efficacy (theoretical)
- Reduces microvascular risk
- Potential for reduced oral antidiabetic medication pill burden
- Can reach desired efficacy quickly

Barriers

- Hypoglycemia
- Weight gain (avg 1 – 3 kg)
- Administration / adherence issues
- Feelings of failure
- Within and between patient variability
- Clinical inertia
- Lack of provider time, support, or training

Diabetes Care 2016;39(Suppl. 1.
Handelsman et al. Endocr Pract 2015;21(Suppl 1):28-29.

History of Insulin



- Highly sought after insulin characteristics
  - *Minimize weight gain*
  - *Reduce number of injections*
  - *Prevent hypoglycemia*
  - *Flexible dosing*

Cahn et al. Lancet Diabetes Endocrinol. 2015;3:638-52.
http://www.diabetes.org/research-and-practice/student-resources/history-of-diabetes.html

Pharmacokinetic Profiles of Basal Insulins

Insulin	Onset (hours)	Peak (hours)	Duration (hours)
Neutral Protamine Hagedorn (NPH)	2-4	4-8	8-12
Detemir	2	---	14-24
Glargine U-100	4-5	---	22-24
Glargine U-300	6	---	36
Degludec	0.5-1.5	---	> 42

Chapter 57. Diabetes mellitus. In: Pharmacotherapy: A Pathophysiologic Approach. 9th ed. 2014.
Toujeo (insulin glargine injection) U-300 [product information]. Bridgewater, NJ: sanofi-aventis; 2015.
Tresiba (insulin degludec injection) [product information]. Plainsboro, NJ: Novo Nordisk Inc.; 2015

Comparisons of Conventional Basal Insulins in T2DM

	NPH vs. glargine U-100	NPH vs. determir	Detemir vs. glargine
Noteworthy findings	• Less nocturnal hypoglycemia with IGlar added to OADs • Rates of nocturnal hypoG was similar when prandial insulin was combined	Less hypoglycemia and weight gain with IDet added to OADs or prandial insulin	• Less weight gain with IDet • Lower insulin doses with IGlar

Iglar=insulin glargine 100 units/mL, IDet=insulin detemir 100 units/mL, OADs=oral antidiabetic agents

Horvath et al. Cochrane Database of Systematic Reviews 2007, Issue 2. Art. No.: CD005613.
Swinnen et al. Cochrane Database of Systematic Reviews 2011, Issue 7. Art. No.:CD006383.
Mannucci, et al. Drug, Healthcare, and Patient Safety. 2015;7:113-20.

Insulin Glargine U-300 Overview

- Post-administration microprecipitate dissolution rate is concentration dependent
- Developed to provide more consistent insulin absorption and longer duration of action than glargine U-100
- FDA approved in February 2015
- Available formulation: insulin glargine U-300 (Toujeo)
- Approved for use in adults with diabetes

Toujeo (insulin glargine injection) U-300 [product information]. Bridgewater, NJ: sanofi-aventis; 2015.

Insulin Glargine U-300 T2DM Clinical Trial Program

Study	Duration	RCT design (non-inferiority)	Treatment
EDITION 1	26 weeks and 26-week extension	Open-label, multinational	Glargine U-300 or glargine U-100 + mealtime insulin ± metformin
EDITION 2	26 weeks and 26-week extension	Open-label, multinational	Glargine U-300 or glargine U-100 + OADs except for sulfonylurea
EDITION 3	26 weeks	Open-label, multinational, insulin-naïve participants	Glargine U-300 or glargine U-100 + OADs (metformin &/or DPP4i)
Baseline: age 58-60 yrs, BMI 30-36, duration of diabetes 9-16 yrs, baseline A1C 8-8.5%			

RCT=randomized control trial; OADs=oral antidiabetic medications; DPP4i=dipeptidyl peptidase-4 inhibitors

Riddle et al. Diabetes Care. 2014;37:2755-62.;; Yki-Jarvinen et al. Diabetes Care. 2014;37:3235-43.;; Bolli et al. Diabetes Obes Metab. 2015;17:386-94
Riddle et al. Diabetolgia. 2014;57:S402.; Yki-Jarvinen et al. American Diabetes Assoication Scientific Sessions; San Fransisco, CA:June 13-17, 2014. Abstract 93-LB.

Insulin Glargine U-300 Study Dose Adjustment Protocol

- Dose adjustment made once weekly

Insulin delivery device could only be adjusted in 3 unit increments

3-day average FBG (mg/dL)	Daily insulin dose adjustment
≥ 140	Increase by 6 units
100 to 139	Increase by 3 units
89 to 99	Continue current dose
< 79	Decrease by 3 units

Riddle et al. Diabetes Care. 2014;37:2755-62.
Yki-Jarvinen et al. Diabetes Care. 2014;37:3235-43.;
Bolli et al. Diabetes Obes Metab. 2015;17:386-94.

Glargine U-300 T2DM Clinical Trial Program Results

	EDITION 1		EDITION 2		EDITION 3	
No. of subjects	811 (26-week) 714 (52-week)		811 (26-week) 629 (52-week)		878	
	U-300	U-100	U-300	U-100	U300	U-100
A1C (%) Mean difference (95% CI)	26-wk: 0.00 (-0.11 to 0.11) 52-wk: -0.17 (-0.20 to -0.05)		26-wk: -0.01 (-0.14 to 0.12) 52-wk: 0.06 (-0.22 to 0.10)		0.04 (-0.09 to 0.17)	
Body weight (kg) Mean change	0.9 increase in both arms (at 26-weeks)		52-wk: 0.42** (0.04 to 0.80) **p=0.0091	52-wk: 1.14 (0.76 to 1.52)	0.4 (SD 3.8)	0.7 (SD 3.8)
Nocturnal hypoglycemia, confirmed or severe Relative Risk (95% CI)	26-wk: 0.76 (0.66 to 0.87) 52-wk: 0.84 (0.75 to 0.94)		26-wk: 0.73 (0.6 to 0.88) 52-wk: 0.63 (0.42 to 0.96)		0.76 (0.59 to 0.99)	

Riddle et al. Diabetes Care. 2014;37:2755-62.;; Yki-Jarvinen et al. Diabetes Care. 2014;37:3235-43.;; Bolli et al. Diabetes Obes Metab. 2015;17:386-94
Riddle et al. Diabetolgia. 2014;57:S402.; Yki-Jarvinen et al. American Diabetes Assoication Scientific Sessions; San Fransisco, CA;June 13-17, 2014. Abstract 93-LB.

Insulin Glargine U-300

- Starting dose
  - *Insulin naïve: 0.2 units/kg daily*
  - *Converting from once daily basal insulin: initiate same unit-per-unit dose*
  - *Converting from twice daily NPH: initiate at 80% of the NPH TDD*
- Administer any time of day, same time every day
- Steady state achieved by day 5, do not adjust dose sooner than every 3 – 4 days
- Higher doses may be required after converting a patient who was previously well-controlled with glargine U-100
- Increases in FBG may occur during the 1st few weeks after converting from glargine U-100 to U-300
- Only available in a disposable prefilled pen
  - *Doses are dialed in 1 unit increments*
  - *Maximum units per injection = 80*
  - *Units per pen = 450*

Toujeo (insulin glargine injection) U-300 [product information]. Bridgewater, NJ: sanofi-aventis; 2015.

Case Study

Mr. James, 52-y/o WM, presents to your community pharmacy with a new prescription for insulin glargine 300 units/mL, metformin 500 mg po BID, and glucometer with testing supplies.

Upon review, you notice the prescriber did not include directions for the insulin (Sig: UTD). Mr. James shares with you that these are both new medications after finding out he has diabetes. He admits to feeling overwhelmed at the doctor's office and doesn't remember the dose he was told to start injecting. Mr. James tells you that his weight was 220 lbs (100 kg) at the office and "everyone kept making a big deal that my A1C is 12".

Which starting dose of insulin glargine U-300 is most appropriate for Mr. James per the AACE/ACE guidelines?

a. 10 units
b. 50 units
c. 20 units
d. 4 units

Case Study

It is now two weeks later and Mr. James returns to your pharmacy to pick up his cholesterol medication. He reports doing well with his new diabetes medications, but he is worried that his blood sugars are still running too high. He denies hypoglycemia and describes appropriate insulin administration technique.

Patient reported fasting BG readings:

Date	Fasting BG (mg/dL)
Today	253
Yesterday	236
2 days ago	261
3 days ago	282
4 days ago	299
5 days ago	278

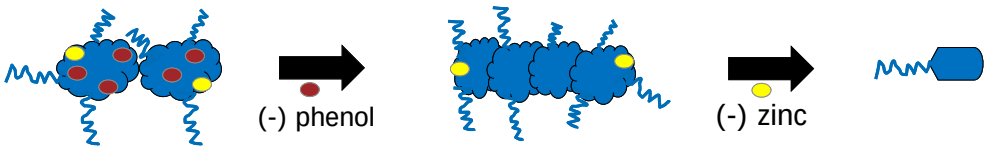
Insulin glargine U-300 dose has been 20 units daily. You offer to call Mr. James's prescriber to determine if an insulin dose change would be authorized.

Select the most appropriate new dose to recommend.

a. 24 units
b. 18 units
c. 30 units
d. Continue current dose, efficacy takes up to 4 weeks

Insulin Degludec Overview

- Ultra-long-acting analog through formation of multihexamers upon subcut injection. Results in slow release of monomers from degludec depot.
- FDA approved in September 2015
- Available formulations: insulin degludec (Tresiba)
  - *100 units/mL (U-100) and 200 units/mL (U-200)*
- Approved for use in adults with diabetes



degludec di-hexamers (in solution)

degludec multi-hexamers (following subcut injection)

degludec monomers (slow absorption)

Tresiba (insulin degludec injection) [product information]. Plainsboro, NJ: Novo Nordisk Inc.; 2015.

Insulin Degludec T2DM Clinical Trial Program

Study	Duration (weeks)	RCT Design (all open-label multinational)	Treatment
BEGIN BASAL-BOLUS T2DM	52	Non-inferiority	Degludec once/day or glargine U-100 + mealtime aspart ± metformin ± pio
BEGIN FLEX	26	Non-inferiority	Degludec flexible (8-40 h intervals) or degludec once/day or glargine U-100 ± oral antidiabetic medications
BEGIN ONCE LONG	52	Non-inferiority, insulin-naïve participants	Degludec once/day or glargine U-100 + metformin ± DPP4-i
BEGIN LOW VOLUME	26	Non-inferiority, insulin-naïve participants	Degludec U-200 once/day or glargine U-100 + metformin ± DPP4-i
BEGIN EARLY	26	Superiority	Degludec once/day or sitagliptin 100 mg ± metformin ± sulfonylurea/glinide ± pio
Baseline: age 58 yrs, mean BMI 30, duration of DM 11 yrs, mean A1C 8.3%8.3%			

Garber et al. Lancet 2012;379:1498-507.; Zinman et al. Diabetes Care 2012;35:2464-71.; Meneghini et al. Diabetes Care 2013;26:858-64.; Gough et al. Diabetes Care 2013;36:2536-42.; Philis-Tsimikas et al. Diabetes Obes Metab. 2013;15:760-66.

Insulin Degludec General Study Dose Adjustment Protocol

- Dose adjustment made once weekly

3-day average fasting BG (mg/dL)	Daily insulin dose adjustment
≥ 162	Increase by 8 units
144 to 161	Increase by 6 units
126 to 143	Increase by 4 units
90 to 125	Increase by 2 units
70 to 89	Continue current dose
56 to 69	Decrease by 2 units If dose > 45 units, decrease by 5%
< 56	Decrease by 4 units If dose > 45 units, decrease by 10%

Garber et al. Lancet 2012;379:1498-507.

Degludec SIMPLE Study Dose Adjustment Protocol

- BEGIN ONCE SIMPLE USE trial randomized patients to either a Simple or Step-Wise titration algorithm
- Degludec was initiated at 10 units once daily
- Participants self-titrated their dose once weekly
- After 26 weeks, all efficacy and safety outcomes were similar between groups

3-day average fasting BG (mg/dL)	Simple Titration	Step-Wise Titration
> 162	Increase by 4 units	Increase by 8 units
145 to 162		Increase by 6 units
127 to 144		Increase by 4 units
91 to 126		Increase by 2 units
71 to 90	Continue current dose	
56 to 70	Decrease by 4 units	Decrease by 2 units
< 56		Decrease by 4 units

Philis-Tsimikas et al. Adv Ther. 2013;30:607-22.

Degludec T2DM Clinical Trial Program Results

BEGIN trial	BASAL-BOLUS T2DM	FLEX		ONCE LONG	LOW VOLUME	EARLY
No. of subjects	1006	687		1030	460	458
A1C (%) Mean difference (95% CI)	0.08 (0.05 to 0.21)	Flex vs gla	Flex vs once	0.09 (-0.04 to 0.22)	0.04 (0.11 to 0.19)	-0.43 (-0.61 to -0.24)
		0.04 (-0.12 to 0.20)	-0.13 (-0.29 to 0.03)			
Body weight (kg) Mean change	Degludec 3.6 Glargine 4.0	Flex 1.5 Once daily 1.6 Glargine 1.3		Degludec 2.4 Glargine 2.1	Degludec 1.9 Glargine 1.5	Degludec 2.3 Sitagliptin -0.4
Nocturnal hypoglycemia Rate Ratio (95% CI)	0.75 (0.58 to 0.99)	0.77 (0.44 to 1.35)	1.18 (0.66 to 2.12)	0.64 (0.42 to 0.98)	0.64 (0.30 to 1.37)	1.93 (0.90 to 4.10)

Insulin Degludec Cardiovascular Outcomes Trial

- Previous meta-analysis of major adverse cardiovascular events (MACE) in 16 Phase 3 degludec trials
  - *Hazard ratio 1.10 (CI 0.68 to 1.77)*
- DEVOTE is an ongoing, multinational, randomized, double-blind study comparing safety of degludec to insulin glargine U-100
  - *Study population: subjects with T2DM (N=7,637)*
    - Age ≥ 50 years with previous CV disease or renal disease
    - Age ≥ 60 years with CV risk factors
  - *Primary outcome: time to 1st MACE*
  - *Study duration: 38 months*
  - *Estimated completion date: September 2016*

Insulin degludec and insulin degludec/insulin aspart NDAs 203314 and 203313.
https://clinicaltrials.gov/ct2/show/record/NCT01959529.

Insulin Degludec

- Starting dose
  - *Insulin naïve: 10 units daily*
  - *Converting from other basal: initiate same unit-per-unit dose*
- Administer any time of day with 8 hours between doses
- Steady state achieved after 2-3 days
- Recommended time between dose increases is 3 to 4 days
- Only available in a disposable prefilled pen
  - *Doses are dialed in 1 unit increments with U-100 pen, 2 unit increments with U-200 pen*
  - *Maximum units per injection: U-100 = 80 units, U-200 = 160 units*
  - *Units per pen: U-100 = 300 units, U-200 = 600 units*

Tresiba (insulin degludec injection) [product information]. Plainsboro, NJ: Novo Nordisk Inc.; 2015

Case Study

Mrs. Albert is 62-y/o BF who has been taking insulin detemir 100 units/mL vials, inject 30 units subQ twice daily, and has received consistent refills of the insulin every month for the past 6 months. She presents at the pharmacy with a new prescription for insulin degludec 200 units/mL inject 60 units subQ daily.

She reports that her blood sugars have consistently been 100-120 every morning for some time, but she really dislikes having to draw up her dose with a vial and syringe. She expresses how happy she is that her insurance will now cover a new insulin that comes in a pen.

Which of the following is true regarding the U-200 insulin degludec 60 units starting dose?

a. It is an appropriate conversion dose based on TDD of detemir (60 units/day)
b. It is too high of a starting dose, should be 80% of detemir TDD (48 units/day)
c. It is too low of a starting dose, should add 4 units to TDD based on SIMPLE titration algorithm (64 units/day)
d. It is too high of a starting dose, should be divided by 2 as the U-200 formulation has been prescribed (30 units/day)

Case Study

Mr. White states that he is concerned about the dose of insulin his provider wants him to start using. He is currently using insulin degludec U-200 and reports that he has been consistent with injecting 40 units every day. His A1C last week was 9.4% and FBG levels have been in the mid-200's every morning upon waking for the past 2 months, He was instructed to increase the insulin dose to 48 units daily. He states: "That's a really big jump in dose, isn't it? ! I think I'll try adding 1 or 2 units instead. What do you think?"

Which of the following is the most appropriate response to address Mr. White's concern?

a. Call your doctor, I cannot advise you on your insulin use.
b. That must be a mistake, adding 8 units is never an appropriate dose increase.
c. Yes, you should only increase by 2 units at a time. That is the only method used when this insulin was studied.
d. That increase represents a 20% change that diabetes experts recommend based on high blood sugar levels like you have been experiencing.

Novel Basal Insulin Summary

- Insulin glargine U-300 and insulin degludec
  - *Comparable glycemic control and changes in weight as glargine U-100*
  - *May reduce risk of nocturnal hypoglycemia compared to glargine U-100**
- Higher doses of insulin glargine U-300 may be required per clinical trial data
- Insulin degludec offers the most flexible dosing of all basal insulins
- Use of degludec U-200 or glargine U-300 may be preferred by patients requiring high-dose insulin
- Degludec and glargine U-300 pre-filled pens require less injection force compared to glargine U-100 pen

*Statistical significance was not consistent across all trials

"Follow-on" Insulin Glargine 100 units/mL

- Identical amino acid sequence, and same pharmaceutical form and strength as insulin glargine U-100
- First insulin approved through an abbreviated approval pathway
- Initial FDA approval in 2000, tentative approval in 2014, final approval December 2015
- Approval was heavily based on efficacy and safety data from other insulin glargine U-100 trials
- Not FDA-approved as a biosimilar product
  - *Would require a reference product licensed under the Federal Food, Drug, and Cosmetic Act*
  - *Insulin glargine 100 units/mL (Lantus) is licensed under the Public Health Service Act*
- Launching December 15, 2016
- Available formulation: insulin glargine U-100 (Basaglar)
- Approved for use in adults and pediatric patients with T1DM, and adults with T2DM

Basaglar (insulin glargine injection [product information]. Indianapolis, IN: Eli Lilly and Company.; 2016
http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm477734.htm

"Follow-on" Insulin Glargine T2DM Clinical Trial

ELEMENT 2 Multinational, multicentre, two-arm, double-blind, parallel, noninferiority study		
Study population	N=756 Uncontrolled on ≥ 2 OADs ± IGlar	
Duration	24-week	
Treatment	LY IGlar or IGlar • 10 units if insulin naïve • Same TTD if entered study on IGlar • Add 1 insulin unit daily until target FBG=100 mg/dL	
A1C (%) Change from baseline: LS mean ± SE LS mean difference (95% CI)	LY IGlar -1.29 ± 0.06	IGlar-1 -1.34 ± 0.06
	0.052 (-0.070 to 0.175)	
Insulin dose (units/kg/day)	0.50 ± 0.03	0.48 ± 0.03
Body weight change (kg)	1.8 ± 0.3	2.0 ± 0.3
Hypoglycemia rate overall (mean ± SD) Nocturnal hypoglycemia	21.3 ± 24.4 7.6 ± 11.8	22.3 ± 28.2 8.1 ± 14.6

OADs=oral antidiabetic medications, LY IGlar=follow-on insulin glargine 100 units/mL, IGlar=insulin glargine 100 units/mL, TDD=total daily dose, FBG=fasting blood glucose, LS=least squares

Rosenstock et al. Diabetes Obes Metab. 2015;17:734-41.

Insulin Glargine Cardiovascular Outcomes Trial

- "Follow-on" insulin glargine used data from ORIGINS CV outcomes study of other insulin glargine U-100 for FDA approval

Intervention	Study population	Duration (Median)	Primary outcomes	Results HR (95% CI)
Insulin glargine 100 units/mL vs. Standard care	N=12,537 Adults age 50 y/o at high-risk for DM (IFG, IGT) or with early T2DM, and with established CVD or at high CV risk	6.2 years (IR 5.8 to 6.7)	• MACE • MACE + revascularization or HF hospitalization	• 1.02 (0.94 to 1.11, p=0.63) • 1.04 (0.97 to 1.11, p=0.27)

HR=Hazard ratio; CI=Confidence interval; MACE=Composite of CV death, nonfatal MI, nonfatal stroke; IFG=Impaired fasting glucose; IGT=Impaired glucose tolerance; IR=Interquartile range; HF=Heart failure

REFERENCES: Please indicate journal name, year, issue/volume, pages (Keep in font size 8)

"Follow-on" Insulin Glargine U-100

- Starting dose
  - *Insulin naïve: 0.2 units/kg/day or 10 units daily*
  - *Converting from other insulin glargine U-100: initiate same unit-per-unit dose*
  - *Converting from glargine U-300 or twice daily NPH: initiate at 80% of the TDD*
  - *Converting from other basal insulins: a change in the dose may be required*
- Administer any time of day, same time every day
- Steady state achieved after 2-3 days
- Recommended time between dose increases is 2 to 3 days
- Only available in a disposable prefilled pen
  - *Maximum units per injection: 80 units*
  - *Units per pen: 300 units*

https://www.basaglar.com/#
Basaglar (insulin glargine injection [product information]. Indianapolis, IN: Eli Lilly and Company.; 2016

Principles of Basal Insulin Use

- "Fix the fasting first"
- Patient self-titration vs. practitioner-directed dose adjustments: exercise clinical judgment
- Avoid overbasalization and target postprandial glucose elevations when basal insulin dose is > 0.5 units/kg/day
- Frequent follow-up with patient necessary until dose is stable

Diabetes Care 2016;39(Suppl. 1.
Carroll et al. Diabetes Care 2002;25:1247-1248.

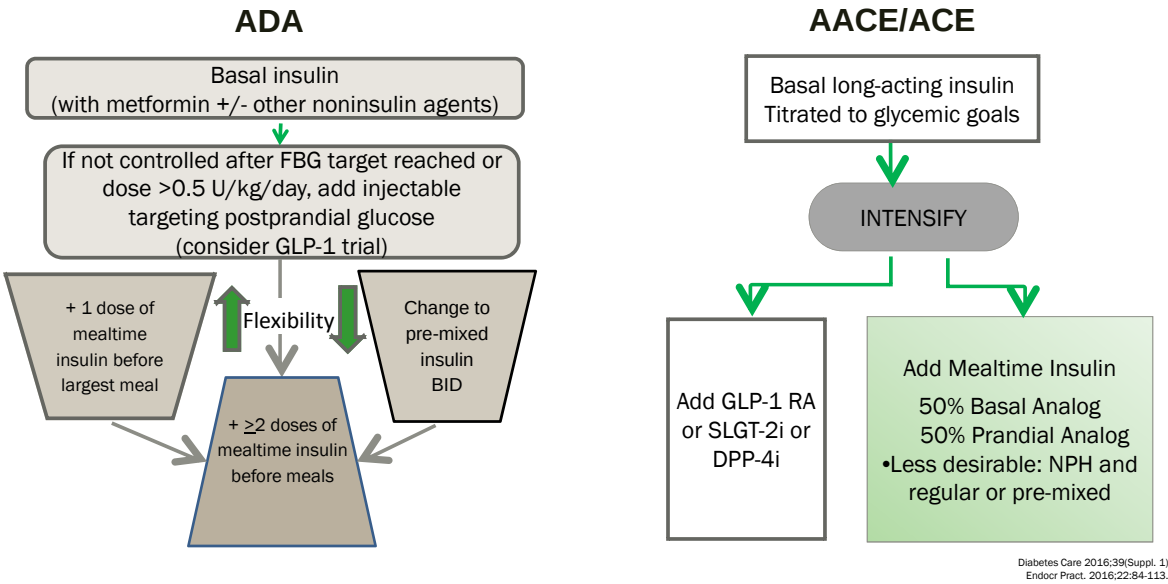
Case Study

A 55-year-old WM has an A1C of 8.5% after 3 months of insulin glargine U-100 up-titration.
Current diabetes medications: insulin glargine 100 units/mL 50 units subQ daily, metformin 1000 mg po BID. Current weight = 95 kg.
Review of glucometer indicates both 3-day and 14-day FBG avg approx. 122 mg/dL.

Which of the following is a potential next step in his treatment that will achieve an A1C goal of < 7%?

a. **Initiate mealtime insulin 4 units subQ with start of largest meal of the day**
b. **Initiate dipeptidyl peptidase-4 inhibitor**
c. **Initiate glucagon-like peptide-1 receptor agonist**
d. **Initiate U-500 regular insulin**

Insulin Intensification Strategies



Diabetes Care 2016;39(Suppl. 1)
Endocr Pract. 2016;22:84-113.

Role of the Pharmacist in Promoting Safe and Effective Insulin Use

- Be a patient advocate
- Spend time with individuals getting 1st insulin prescription
  - *Address patient's questions, concerns, or misconceptions*
  - *Discuss expectations of therapy*
  - *How and when to self-monitor blood glucose levels*
  - *Lifestyle modifications*
  - *Identification, management, avoidance of hypoglycemia*
  - *Sick day management*
- Repetitive counseling appropriate insulin product preparation and injection technique
  - *Optimal administration times (with or without food, morning vs. evening)*
  - *Discuss storage*
  - *Use teach back method*
  - *Demonstration devices will be helpful*
- Specialty training programs in diabetes management
  - *CDE, BC-ADM*
  - *APhA certificate training program*

Additional Resources

- Specialty training programs in diabetes management
  - *CDE, BC-ADM*
  - *APhA certificate training program*
- American Diabetes Association
  - *www.diabetes.org*
- American Association of Clinical Endocrinologist
  - *www.aace.com*
- American Association of Diabetes Educators
  - *www.diabeteseducator.org*
- National Diabetes Education Programs
  - *http://www.niddk.nih.gov/health-information/health-communication-programs/ndep/Pages/index.aspx*

Case Study

Mr. Kelly, a 58-y/o BM, is one of your regular patients.

PMH: resistant HTN, T2DM, Proliferative diabetic retinopathy.

You have concerns about Mr. Kelly's health literacy after numerous conversations about his poor medication adherence. You have explained to him that his chronic medications have plenty of refills and he just needs to request them when they are due or they can be set up on the auto-refill system. Despite these past conversations, he still thinks his prescriber's office has to order the medications each time.

You also notice that he is squinting and looking confused when you show him a Rx bottle to point out where the pharmacy phone number is and where the current remaining refills are.

Current diabetes medications: insulin glargine 100 units/mL vial 45 units, metformin 1000 mg po BID

What intervention can you make to facilitate Mr. Kelly's safe and effective use of insulin?

Meet KD, a 57-year-old WF.....

- Presenting for DM disease state management at the family medicine clinic. She has a 10-year history of diabetes.
- On metformin 1000 mg po BID since her diagnosis and glipizide was increased to 10 mg po BID 3 months ago.
- She reports monitoring home fasting BG most days with all levels between 250 mg/dL and upwards of 300s.
- She was resistant to the idea of insulin 3 months ago (at 1st Pharm.D. encounter with patient).
- Encounter note from PCM 3 weeks ago indicates insulin was discussed and patient is now ready to start it, initiation deferred to Pharm.D. service.

KD case, continued

- Other medical problems: HTN, asthma, OSA, peripheral neuropathy
- Other medications: atorvastatin 80 mg/day, lisinopril 20 mg po daily, gabapentin 300 mg po TID, albuterol HFA 2 puffs Q 4-6 h
- Ht 5 ft. 8 in., Wt 126 kg, BMI 42.3 kg/m^2
- Vitals

Today	2 months ago
BP 126/80 mmHg, HR 68 bpm	142/80 mmHg, HR 70 bpm

- A1C 10.8% as of 1 week ago, down from 11.3% 3 months ago
- All other labs within normal limits, SCr 0.76 mg/dL

Question 1

Which of the following is an indication for KD to start insulin according to the American Association of Clinical Endocrinologists? SELECT ALL THAT APPLY

a. **A1C goal not achieved after 3 months of dual therapy**
b. **A1C > 7.5% and taking dual noninsulin therapy**
c. **A1C > 9% regardless of symptoms**
d. **T2DM diagnosed 10 years ago**

Question 2

Which of the following is the most appropriate diabetes therapy change for KD?

a. Initiate basal insulin 0.5 units/kg/day
b. Initiate basal and mealtime insulin (TDD 0.5 units/kg/day, 50% basal and 50 % mealtime)
c. Initiate basal insulin 0.2 units/kg/day
d. Initiate basal 0.2 units/kg/day and increase glipizide to 20 mg po BID

KD returns 6 months later with a Rx for glucagon

- Her A1C has decreased; however, she is having "night sweats" about 4 times per week in the middle of the night
- Has been eating a bedtime snack to try to prevent, but the problem is still occurring
- Reports good adherence, administers at the same time daily
- Her primary care provider has been altering insulin dosages to limit these night time hypoglycemic reactions but has not had success

Medications include:

- Metformin 1000 mg BID x 10 years
- Lantus 60 units at bedtime daily
- Stopped glipizide due to hypoglycemia

Question 3

Which therapy would be an option for KD to gain glucose control and potentially avoid hypoglycemia?

a. Start inhaled insulin at 24 units TID
b. Continue all medications and initiate insulin aspart 70/30 pre-mix
c. Switch glargine U-100 to glargine U-300 or insulin degludec
d. Switch glargine U-100 to "follow on" glargine U-100

Take home points

- Insulin initiation can be considered at any stage of T2DM treatment with once-daily basal insulin added to OADs using weight-based dosing (for NPH, glargine, and detemir) or 10 units for degludec.
- Patient-specific parameters/preferences should drive shared decision-making and medication selection.
- Insulin glargine U-300 and insulin degludec may be preferred in patients with a history of severe and/or frequent nocturnal hypoglycemia with other basal insulins
- Frequent patient follow-up is necessary when initiating insulin therapy or for poor glycemic control with dose titrations as often as once to twice weekly.

IPhA Annual Conference
Pre-conference Symposium
September 29, 2016

Advanced Clinical Management in Diabetes Care

Basal Insulin: Initiation of Insulin and Advanced Management

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IPhA Annual Conference
Pre-conference Symposium
September 29, 2016

Advanced Clinical Management in Diabetes Care

Sneha Srivastava, PharmD, BCACP, CDE
Lalita Prasad-Reddy, PharmD, MS, BCPS, BCACP, CDE

Disclosure and Conflict of Issue

- The speakers of this CE have no conflict of issues to disclose.

OBJECTIVES

- Discuss FDA regulations for blood glucose monitoring device standards.
- Compare and contrast glucose monitoring options and drug delivery devices available to aid in adherence and better self-efficacy of disease state control.
- Describe strategies to increase shared decision making with patients regarding diabetes management.
- Explore appropriate self-care counseling considerations for patients with diabetes.

Sweet Gal

- Mrs. Sweet Gal is your 52 year old patient – she has been coming to your pharmacy to pick up her medications for years. Throughout this time, you have chatted with her frequently. Today she tells you she's been told her diabetes is getting worse and although it did shock her at first, she is choosing to address it differently now.

- Medication List
  - Metformin 1000mg twice daily (misses second dose often – evenings get hectic)
  - Sitagliptin100mg daily
  - Aspirin 81mg daily
  - Atorvastatin 40mg every night (misses often for same reason)

- Current A1C = 10.2% Previous A1C = 9.4% (3 months ago), 8.2% (6 months ago)

- Currently checking blood glucoses 1 – 2 times a week
- She is open to the idea today of intensifying her therapy, but she does admit adherence will be an issue (due to her busy lifestyle), in addition to her fear of needles.

Question 1

Considering that Sweet Gal is open to initiating insulin, how often should she check her glucose according to the CMS guidelines?

A. Three times daily
B. When she feels "low"
C. Once daily
D. At bedtime

Question 2

- Which of the following represents shared decision making?
  - *A. It is the responsibility of both the patient and HCP to provide information and make decisions*
  - *B. It is the responsibility of the patient to provide information so the HCP can make the best decision.*
  - *C. It is the responsibility of the HCP to give information so the patient can make the best decision.*
  - *D. The patient gives information and makes the decision that works best for them; the HCP ensures that it will not harm the patient.*

Blood glucose monitoring

- Major tool to assess diabetes **self**-management
  - *Allows for real-time assessment of glucose*
  - *Allows for self-adjustment of medications through problem solving*
  - *Notifies, and can even prevent, episodes of hypoglycemia*
  - *Can be utilized for pattern management for long-term control of diabetes*
  - *Can provide POSITIVE reinforcement for the effects of nutrition, exercise, and lifestyle factors on blood glucose*

Recommendations for Self-Monitoring of Blood Glucose (SMBG)

Patients on *intensive* insulin therapy

- Prior to meals and occasionally post-prandial
- Bedtime
- Prior to exercise
- When hypoglycemia is a concern as well, as well as post-hypoglycemia treatment
- Prior to critical tasks

Patients using basal insulin or oral agents

- Evidence is insufficient, so SMBG should be utilized as a guide

American Diabetes Association. Standards of medical care in diabetes—2016. *Diabetes Care.* 2016;39(suppl 1):S1-S106.

CMS Coverage for SMBG

Insulin-Dependent Patients

- Medicare provides coverage for up to 100 test strips and lancets every month

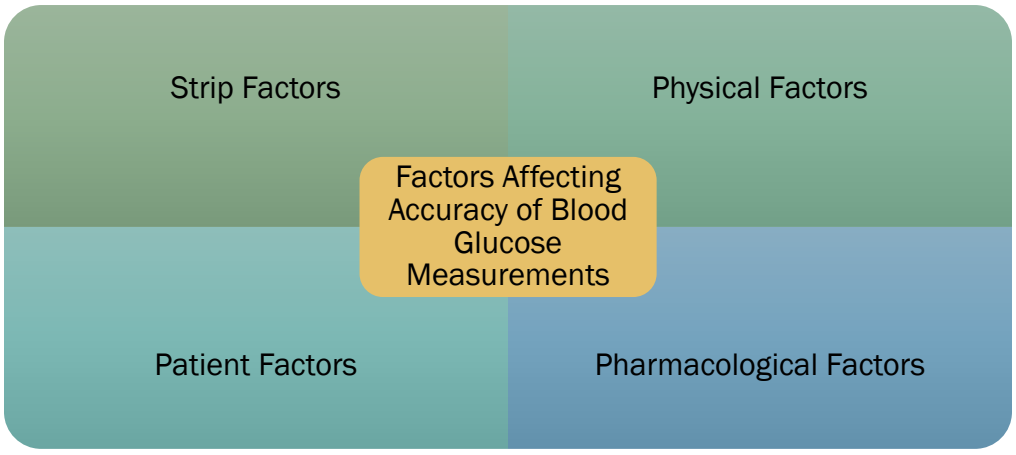
Non-Insulin Dependent Patients

- Medicare provides coverage for up to 100 test strips and lancets every month

More supplies if deemed medically necessary

https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/downloads/SE1008.pdf

Affecting Factors



J Diabetes Sci Technology; 2009;3(4):903-13.

Factors

- **Strip Factors**
  - *Alterations in enzyme material*
  - *Exposure to high temperature*
  - *Lifetime of strip*
- **Pharmacological Factors**
  - *Sugar substances*
  - *Dialysis fluids*
  - *Acetaminophen*
  - *Ascorbic acid*

J Diabetes Sci Technology; 2009;3(4):903-13.

Factors

- **Physical Factors**
  - *Altitude*
  - *Temperature*
    - Alterations can be as great as 10%, and can either be positive or negative
- **Patient Factors**
  - *Coding*
  - *Variations in RBC indices*
  - *Patient technique*
  - *Co-morbid conditions*
    - Hyperlipidemia, COPD

J Diabetes Sci Technology; 2009;3(4):903-13.

How Accurate is My Meter?

- Meters typically will claim an average error rate of < 5%

Best class meters

- Inaccuracy rates of 5.5 - 7%

Slightly less accurate meters

- Inaccuracies of 7 – 8.5%

Least accurate meters

- Inaccuracy > 8.5%

J Diabetes Sci Technology; 2009;3(4):903-13.

FDA Regulations For Glucometers

Meters for In-Home Use

+/- 15% in-home use

- 95% of values must be within this range
- Readings should be reliable from 50 – 400 mg/dL

Meters for In-Clinical Settings

+/- 10% in-clinic usage

- 99% of values must be within this range
- Smaller threshold for hypoglycemic values
- Readings should be reliable from 10 – 500 mg/dL
- Enhanced recommendations for cleaning and disinfection

http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm380325.pdf)
http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm380327.pdf

A Focus on Patient Adherence: New Drugs and Delivery Devices

Continuous Glucose Monitoring (CGM)

- Measures interstitial fluid glucose levels to provide semi-continuous information about glucose levels
  - *Identifies fluctuations that would not have been identified with conventional self-monitoring*
  - *Two types of CGM systems : retrospective and real-time*

	PROS	CONS
SMBG	•Fast •Requires small amount of blood •Reasonably accurate	•Each meter varies in characteristics
CGM	•When utilized appropriately can reduce risk of hypoglycemia and lower A1C	•Has a lag time between plasma and interstitial glucose •Some concerns with accuracy

Diabetes Care. 2005;2895): 1231-39.

Continuous Glucose Monitoring

- Provides early notification of highs and lows
- Can help provide direction as to blood glucose
- Alerts for out-of-range glucoses while sleeping
- Provides at-a-glance glucose readings
- Assists in analyzing glucose patterns

Diabetes Care. 2005;2895): 1231-39.

AACE Recommendations for Personal CGM

"Good" Candidates

- Patients who are Type 1
  - A1C levels >7% and able to use the device near-continuously
  - Type 1 diabetes with hypoglycemia unawareness or frequent hypoglycemia
  - Hyperglycemia over target or with excessive glycemic variability
  - Requiring A1C lowering without excessive hypoglycemia (eg, potentially disabling or life-threatening)
  - Preconception and pregnancy

Other Candidates

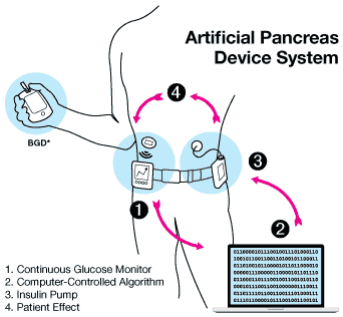
- Youth who frequently monitor their BG levels
- Committed families of young children (<8 years of age), especially if there are problems with hypoglycemia
- Patients with Type 2 Diabetes needing improved control of glycemia
- Intermittent CGM may be useful in patients with dawn phenomenon, or hypoglycemic unawareness

2- to 4-week trial recommended

Endocrine Practice. 2010; 16(5): 1-16. Accessed at https://www.aace.com/files/continuousglucosemonitoring.pdf

Artificial Pancreas (The Closed-Loop)

- Technological system consisting of a continuous glucose monitor, insulin pump, glucometer, and computer system
- Led by a computer-controlled algorithm that connects the CGM and insulin pump and allows for continuous real-time communication
  - *Based upon current blood glucose, or predictive equations, will allow for automatic insulin bolusing from pump*



Diabetes. 2011; 60(11): 2672-82.

Factors Associated with Non-Adherence to Insulin Therapy

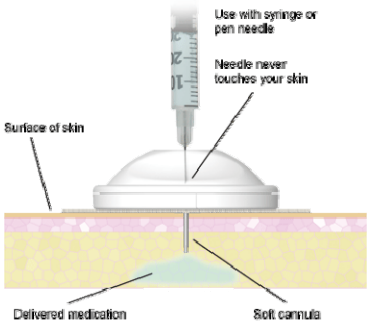
- Time
- Embarrassment
- Forgetfulness
- Sickness
- Fear of hypoglycemia
- Difficulties in preparing injection
- Shortage
- Pain
- Weight gain
- Feeling worse after injections

http://emrc.tums.ac.ir/upfiles/186318109.pdf

Pak J Med Sci. 2014 Mar-Apr; 30(2): 233–239.

I-PORT

- Removes pain from multiple insulin injections
  - *No direct injection of medication into skin*
- Cannula remains under skin for up to three days
  - *Medication is injected into the insertion device, and travels through cannula into subcutaneous tissue*
- Reduces the overall number of skin punctures
  - *Does not reduce overall number of insulin injections however!*
- Suitable for adults and children and remains on the body while bathing, sleeping, and exercising.
- Can accommodate up to 75 injections in 72 hours



No needle remains under the skin

Am Health Drug Benefits. 2010; 3(2): 117–122.
http://www.medtronicdiabetes.com/products/i-port-advance

Patient Perceptions of I-PORT

- Reduced anxiety
- Improved potential compliance
- Decreased pain

Standard vs. Injection Port

Endocrine Disease. 2007; 1: 32–33

I-Port: Clinical Data

Trial Design	Patient Population	Results: Glucose Control	Results: Patient Perceptions
Multicenter, randomized, prospective, controlled, open-label, two-period crossover design	Patients who were treated with intensive, multi-injection insulin therapy using regular human or rapid-acting insulin and insulin glargine were randomly assigned to: 1) Standard injection (n=18) 2) Single I-Port device (n=20) 3) Two separate I-Port devices (Dual I-Port) (n=36)	Participants' glycosylated albumin was not significantly different between SI, single I-Port, and Dual I-Port treatment regimens (P = 0.99 for SI vs. single I-Port and P = 0.97 for single I-Port vs. Dual I-Port). Fifty of 72 participants (69.4%) reported that the I-Port was useful and helpful in the management of their diabetes.	A significantly larger number of subjects (62.5% SI vs. 48.1% I-Port) reported that it was hard to stay in control of diabetes during the SI than during the I-Port treatment (P = 0.016). Additionally, a significantly number of subjects (68.7% I-Port vs. 61.1% SI) rated their overall health very good or excellent when using the I-Port than when using SI (P < 0.001).

Diabetes Spectrum 2008 Jul; 21(3): 197-202.

V-GO®

- Disposable insulin delivery device approved for use in patients with Type 2 Diabetes Mellitus
- Filled with a rapid-acting insulin, it provides a set basal fixed ratio, with on-demand "clicks" for boluses
  - *1 click = 2 units of rapid-acting insulin*
- Wearable for 24-hours, and does not contain a heavy-duty infusion set
  - *Patient friendly vs. traditional insulin "pumps"*
  - *Limited basal infusion rate – ranging from 20 – 40 units/24 hours*

http://www.go-vgo.com/hcp/dosing-information

V-GO® – How it Works

http://www.go-vgo.com/hcp/dosing-information

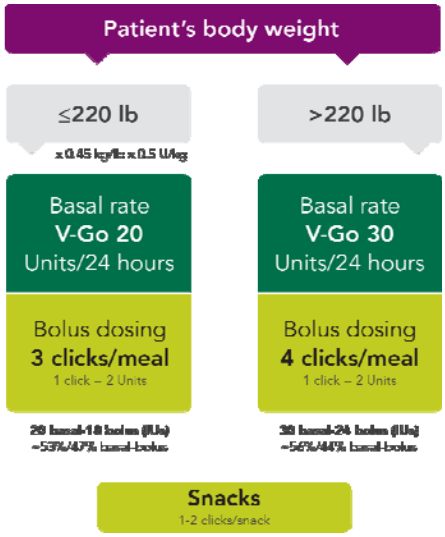
V-GO® Characteristics

- Designed to release a set basal rate throughout the day once the needle is injected
- Allows patients on-demand bolus insulin with meals or as correction
- Waterproof, spring-loaded device containing only rapid-acting insulin that runs without the use of batteries or computer software
- Bolus insulin filling
  - *Can be filled with Humalog® for up to 24 hours prior to use if refrigerated or if left at room temperature*
  - *Can be filled with NovoLog® for up to 5 days prior to use if refrigerated; up to 3 days prior to use if left at room temperature*
- Must be changed every 24 hours

J Diabetes *Sci Technol . 2015 ;9 (5): 1111-1116*
http://www.go-vgo.com/hcp/dosing-information

V-Go® Dosing and Titration

V-Go option	Preset basal rate	+	On-demand bolus dosing	=	Total available insulin
VGO® 20 DISPOSABLE INSULIN DELIVERY	20 Units/24 hr (0.83 U/hr)	+	Up to 36 Units in 2-Unit increments*	=	56 Units
VGO® 30 DISPOSABLE INSULIN DELIVERY	30 Units/24 hr (1.25 U/hr)	+	Up to 36 Units in 2-Unit increments*	=	66 Units
VGO® 40 DISPOSABLE INSULIN DELIVERY	40 Units/24 hr (1.67 U/hr)	+	Up to 36 Units in 2-Unit increments*	=	76 Units



http://www.go-vgo.com/hcp/dosing-information

Patient Results– V-Go®

Three-month prospective active comparator study to observe A1C lowering effects of multiple daily insulin injections (MDII) versus the use of the V-Go® insulin delivery system for patients with uncontrolled type 2 diabetes mellitus with an A1C > 8%

the effect on insulin requirement for these patients was assessed with secondary comparisons of weight, blood pressure, prevalence of hypoglycemic events, and quality of life before and after 3 months of intensified insulin therapy with regular monitoring by a clinical pharmacist at an internal medicine clinic.

MDII (n = 3)	V-GO® (n = 5)
Baseline A1C for MDI group was 8.8%. Average A1C change in the 3 patients in the MDII group was an increase of 0.2%, resulting in an end-average of 9.0%	Baseline A1c for V-GO group was 9.1%. The average A1C lowering experienced by patients in the V-Go group was 1.5%, resulting in a post–study average A1C of 7.5%.
All patients in the MDII group experienced an increase in insulin total daily dose (TDD) with an average of 15 units daily to achieve therapeutic goals	All patients in the V-Go group experienced a decrease in insulin TDD, with an average decrease of 26.3 units.

J Diabetes Sci Technol . 2015 ;9 (5): 1111-1116

Other Agents in the Pipe-Line

CeQur PAP®

- Three-day disposable insulin device designed for patients with type 2 diabetes mellitus
- Provides injection free bolus with a push of a button
- Provides patients a notification when reservoir needs to be replaced
- Can delivery up to 330 units in three days
- More options for basal preset doses

Johnson and Johnson One Touch Via®

- Three-Day disposable insulin device designed for patients with Type 1 and Type 2 Diabetes
- Allows for dosing of 2-unit increments of rapid acting insulin
- Lightweight and discrete
- Allows for up to 200 unit delivery in a 3 day period
- Does not provide basal delivery of insulin

http://diatribe.org/jjs-onetouch-mealtime-insulin-delivery-device-first-look-its-artificial-pancreas-device http://www.cequrcorp.com/cequr-paq/

SHARED DECISION MAKING

Treatment Decision Making Options

- Informed patient
  - Clinician → information → Patient ← Makes decision
- Paternalistic approach
  - Makes decision → Clinician ↔ Information ↔ Patient
- Shared decision making
  - Clinician ↔ Information and Decision Making ↔ Patient

Shared Decision Making (SDM) and Available Tools

- Definition: “approach where clinicians and patients share the best available evidence when faced with the task of making decisions, and where patients are supported to consider options, to achieve informed preferences”
- Approaches
  - Information
  - Choice
  - Conversation
- Available tools
  - Decision aids
  - Decision board

Elwyn

Examples of Decision Aids

Considerations in SDM and Diabetes

- Progression of condition
- Setting of decision making
- Opportunity to make decisions
- Reversibility of decision
- Nature of choice
- Treatment characteristics
- Necessary specialized knowledge
- Administration control
- Treatment/monitoring
- Role of adherence
- Social impact
- Outcome

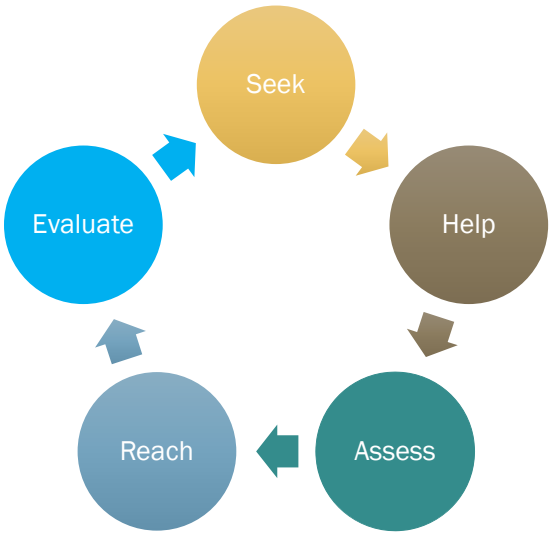
http://onlinelibrary.wiley.com/doi/10.1111/j.1369-7625.2006.00359.x/full

Challenges with SDM

- Duration of patient visit
- Long periods of time in between visits
- Encounters with different health care providers
- Skills/training of personnel
- Cost

http://onlinelibrary.wiley.com/doi/10.1111/j.1369-7625.2006.00359.x/full

SHARE Approach



http://www.ahrq.gov/sites/default/files/wysiwyg/professionals/education/curriculum-tools/shareddecisionmaking/tools/tool-8/share-tool8.pdf

AADE7 Self-Care Behaviors™

- Healthy eating
- Being active
- Monitoring
- Taking medication
- Problem solving
- Reducing risks
- Healthy coping

https://www.diabeteseducator.org/patient-resources/aade7-self-care-behaviors

Healthy Eating and Being Active

Nutrition

- Healthy meal planning
  - Macro and micronutrients
  - Measuring servings
- Reading nutrition labels
- Plate method

Physical activity

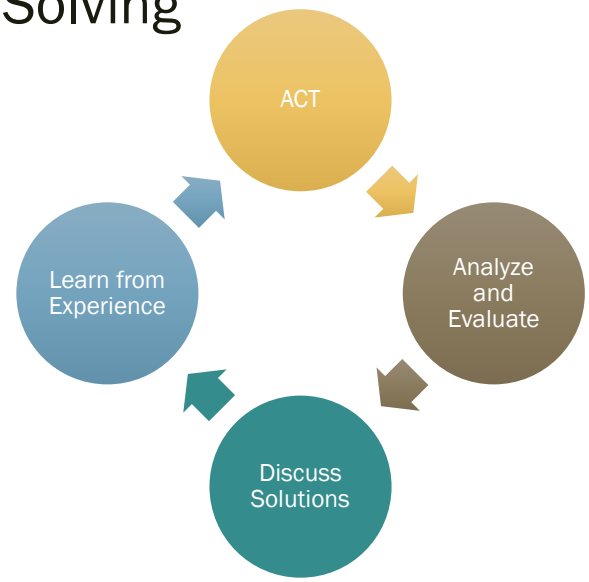
- Examples of increasing activity throughout the day
- Three 10 minute sessions throughout the day = One 30 minute session

Taking Medications

- Why am I taking these medications?
- What will they do for me?
- How should I fit them into my schedule?
- Will they cause adverse effects?
  - *If so, what do I do?*

REFERENCES: Please indicate journal name, year, issue/volume, pages (Keep in font size 8)

Problem Solving



https://www.diabeteseducator.org/patient-resources/aade7-self-care-behaviors/problem-solving

Reducing Risks

- Smoking Cessation
- Physician's visits
- Dental examinations
- Foot Care

Healthy Coping

- Being active
- Pursuing hobbies
- Participating in faith based activities
- Attending support groups

Sweet Gal

- Mrs. Sweet Gal is your 52 year old patient – she's been coming to your pharmacy to pick up her medications for years. Throughout this time, you have chatted with her frequently – today she tells you she's been told her diabetes is getting worse and although it did shock her at first, she choosing to address it differently now.

- Medication List
  - Metformin 1000mg twice daily (misses second dose often – evenings get hectic)
  - Sitaglipitin 100mg daily
  - Aspirin 81mg daily
  - Atorvastatin 40mg every evening (misses often for same reason)

- Current A1C = 10.2% Previous A1C = 9.4% (3 months ago), 8.2% (6 months ago)

- Currently checking blood glucoses 1 – 2 times a week
- She is open to the idea today of intensifying her therapy, but she does admit adherence will be an issue (due to her busy lifestyle), in addition to her fear of needles.

Question 1

Considering that Sweet Gal is open to initiating insulin, how often should she check her glucose according to the CMS guidelines?

A. Three times daily
B. When she feels "low"
C. Once daily
D. At bedtime

Question 2

- Which of the following represents shared decision making?
  - *A. It is the responsibility of both the patient and HCP to provide information and make decisions*
  - *B. It is the responsibility of the patient to provide information so the HCP can make the best decision.*
  - *C. It is the responsibility of the HCP to give information so the patient can make the best decision.*
  - *D. The patient gives information and makes the decision that works best for them; the HCP ensures that it will not harm the patient.*

Take home points

- Blood glucometer regulations have tightened, with clinical meters needing more accuracy for point of care decision making
- Continuous glucose monitoring can be utilized with SMBG to provide up-to-date and proactive methods to blood glucose management
- Novel agents for insulin delivery may improve overall patient adherence, and enhance clinical outcomes
- Shared decision making is an important component of diabetes management, and research shows that individuals who are involved in DSME have improved control of their disease

IPhA Annual Conference
Pre-conference Symposium
September 29, 2016

Advanced Clinical Management in Diabetes Care

Sneha Srivastava, PharmD, BCACP, CDE
Lalita Prasad-Reddy, PharmD, MS, BCPS, BCACP, CDE

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IPhA Annual Conference
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Advanced Clinical Management in Diabetes Care

Diabetes Medical Nutrition Therapy: The Role of the Pharmacist

Anne Daly, MS, RDN, BC-ADM, CDE
SIU School of Medicine Center for Family Medicine

Disclosure and Conflict of Issue

- Ms. Anne Daly has no conflicts of interest to report

REFERENCES: Please indicate journal name, year, issue/volume, pages (Keep in font size 8)

OBJECTIVES

- Review evidence based nutrition therapy recommendations for managing diabetes.
- Discuss the role of pharmacists in the delivery of the nutrition component of diabetes self-management and support.
- Review recent position paper on diabetes self-management education and support in type 2 diabetes, including when, what and how these services should be provided.
- Identify common nutrition topics of interest, including the use of sweeteners, net carbs and cooking oils.

Nutrition Therapy Recommendations for Management of Adults with Diabetes

- See handout
- 2014 Position Statement published in Diabetes Care

REFERENCES: Evert et al. Diabetes Care 2014 37(1)

Medical Nutrition Therapy (MNT) Effectiveness in Patients with Diabetes

- Glycemic Control
  - ~1% ↓ A1c in newly diagnosed T1DM
  - ~2% ↓ A1c in newly diagnosed T2DM
  - ~1% ↓ A1c with average 4 year duration T2DM
  - 50-100mg/dl ↓ Fasting Blood Glucose
  - Outcomes known 6 weeks – 3 months
- Lipid
  - 10-13% ↓ Total cholesterol (24-32mg/dl)
  - 12-16 %↓ LDL cholesterol (15-25mg/dl)
  - 8% ↓ Triglycerides (15-35mg/dl)
  - Without physical activity, HDL ↓ by 7%; with physical activity, no ↓
- Hypertension
  - 5mmHg ↓ systolic blood pressure, 2mmHg ↓ diastolic blood pressure in HTN patient

REFERENCES: Diabetes Care 2014 37(1):S120-143.

Benefits Associated with DSME/S

Benefits
• **Improved health outcomes** ① Reduced A1c by as much as 88% ❷ Reduced onset and/or advancement of complications ③ Reduced hospital admissions and readmissions
• **More healthful eating patterns and regular activity**
• **Enhances self-efficacy and empowerment** ① Increased healthy coping ❷ Improved quality of life
Note: 1) Benefits of education decrease over time, 2) sustained improvements require time and follow-up, and 3) effectiveness directly correlated to amount of time spent with educator.

DSME/S = Diabetes Self-Management Education & Support

REFERENCES: Powers MA et al. DSME/S Position Statement 2015 Diabetes Care, The Diabetes Educator, Journal of Academy of Nutrition and Dietetics.
Norris SL, et al. Diabetes Care 2001.

Role of the Pharmacist

- Diabetes Self-Management Education/Support
- Medical Nutritional Therapy

AADE Practice Levels

- Level 1: Beginner / Advanced Beginner /Basic
- Level 2: Competent / Proficient / Intermediate
- Level 3: Expert / Advanced

REFERENCES: AADE Practice Levels for Diabetes Educators and Diabetes Paraprofessionals 2016.

Level 1: Diabetes Educator

- Beginner/ Advanced Beginner / Basic
- Licensed or Registered Pharmacist
- 0-2 years direct care experience in diabetes

REFERENCES: AADE Practice Levels for Diabetes Educators and Diabetes Paraprofessionals 2016.

Level 2: Diabetes Educator

- Competent / Proficient / Intermediate
- Experienced Clinician/CDE
- 3-5 years post-achievement as CDE

REFERENCES: AADE Practice Levels for Diabetes Educators and Diabetes Paraprofessionals 2016.

Level 3: Diabetes Educator

- Expert / Advanced
- BC-ADM/CDE/FAADE/Expert
- > 5 years direct engagement in diabetes as specialty practice
- Demonstrates autonomous, assessment, problem solving, planning, implementation, evaluation of diabetes care.
- Includes 6 professional categories, must meet at least 2; CE, presentations, publications, research, preceptorships, professional service considered for BC-ADM renewal
- BC-ADM credential now administered by AADE

REFERENCES: AADE Practice Levels for Diabetes Educators and Diabetes Paraprofessionals 2016.

Competencies for Diabetes Educators & Diabetes Paraprofessionals

- Domain 1: Pathophysiology, Epidemiology, and Clinical Practice of Prediabetes and Diabetes
- Domain 2: Culturally Competency Across the Lifespan
- Domain 3: Teaching and Learning Skills
- Domain 4: Self-Management Education
- Domain 5: Program and Business Management

REFERENCES: AADE Practice Levels for Diabetes Educators and Diabetes Paraprofessionals 2016.

DSME/S Content Areas

- Describing diabetes disease process & treatment options
- Incorporating nutritional management into lifestyle
- Incorporating physical activity into lifestyle
- Using medications safely & for maximum therapeutic effectiveness
- Monitoring blood glucose + other parameters, interpreting and using results for self-management decision making.
- Preventing, detecting and treating acute complications.
- Preventing, detecting and treating chronic complications.
- Developing personal strategies to address psychosocial issues and concerns.

REFERENCES: Haas et al. Diabetes Care 36(1):S100-108. 2013

Role of the Pharmacist in Nutrition Education : Key Component of DSME

- Perform nutrition screening as part of the DSME assessment
- Refer for individualized MNT by RD or group DSMT as needed
- Document findings from diabetes assessment and nutrition screening in electronic medical record.

eat right. Academy of Nutrition and Dietetics

REFERENCES: Daly et al. JI Am Diet Assoc 103(3):528-539. 2009

Role of the Pharmacist: Nutrition Screening as Component DSME

- Has patient had any previous education about how to eat – when, where, by whom?
- What does the patient do differently, if anything, regarding eating because they know they have diabetes?
- Does the patient understand what healthy eating means?
- What/when/where is the patient eating currently?
- Do current eating behaviors resemble diabetes nutrition therapy recommendations, or are changes indicated?
- Are food resources adequate? If not, are they aware of support services?
- If blood glucoses are out of target range, are poor food choices a factor?

Role of the Pharmacist: Basic Nutrition Education Topics

- Consistent timing of meals
- Healthy eating / good nutrition – ie: Plate Method, Food Pyramid
- Effects of carbohydrate on glycemic control
- Heart health eating – reducing fat and sodium
- Reading food labels, how to use information
- Use of sweeteners and alcohol
- Eating away from home
- Sick days – food and fluid intake

REFERENCES: Daly et al. JI Am Diet Assoc 109(3):528-539. 2016

Medical Nutrition Therapy Provided by RDs: Nutrition Care Process

- Nutrition referral from PCP
- Nutrition assessment using diabetes Nutrition Practice Guidelines
- Nutrition diagnosis using standardized terminology
- Nutrition intervention
- Nutrition monitoring & evaluation (includes changes in MNT as needed) Nutrition documentation
- Outcomes data management.

RD REGISTERED DIETITIAN NUTRITION FACTS FROM THE EXPERTS

REFERENCES: Daly, et al. JI Am Diet Assoc. 109(3):528-539. 2009

Overview of Medical Nutrition Therapy: (MNT)

- **MNT:** evidenced-based application of nutrition care process provided by RD
- **Includes:**
  - Individual assessment, nutrition diagnosis, intervention/monitoring
- **CMS reimburses for diabetes MNT when provided by qualified provider.**
- **Characteristics of MNT:**
  - Series of 3-4 encounters with RD from 45-90 minutes; additional sessions may be needed
  - Should begin at diagnosis or at 1st referral to RD, completed within 3-6 months
  - At least 1 follow up encounters is recommended to enforces lifestyle changes
  - Individualized modification of food plan/physical activity/medication dosing for improved outcomes
  - Specific modifications to macronutrients, sodium to improve lipid and hypertension goals, celiac disease, gastroparesis, eating disorders, kidney disease, etc.

REFERENCES: Powers MA, et al. DSME/S Position Statement 2015. Diabetes Care, The Diabetes Educator, Journal of Academy of Nutrition and Dietetics.

DSME/S in Type 2 Diabetes

PURPOSE:
1. Improve patient experience of care/education
2. Improve health of individuals & Populations
3. Reduce diabetes-associated per capita health care costs

Provide HC teams with information required to better understand the education process

Provides a diabetes education algorithm that defines when, what and how DSME/S should be provided for adults with type 2 diabetes

Diabetes Self-management Education and Support in Type 2 Diabetes: A Joint Position Statement of the American Diabetes Association, the American Association of Diabetes Educators, and the Academy of Nutrition and Dietetics

Diabetes Care 2015;38:1372–1382 | DOI: 10.2337/dc15-0730

REFERENCES: Diabetes Care 2015;38(7):1372-1382

Unacceptable State of DSME/S

- 6.8% of newly diagnosed T2DM with private insurance received DSME/S within 12 months of diagnosis
- 4% of Medicare participants received DSME/S and/or MNT

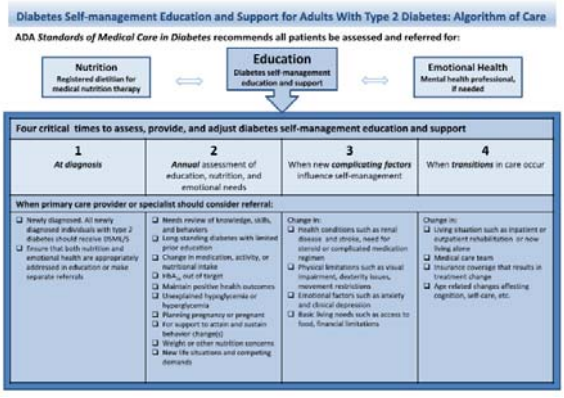
REFERENCES: Duncan et al. Diab Educ. 2009;35:725-760
Li et al. MMWR. 2014.63:1045-1049

DSME/S Algorithm of Care

- 4 Critical times to assess, provide and adjust
  - ❶ At Diagnosis
    - All Individuals with Type 2 diabetes
    - Include emotional health and nutrition
  - ❷ Annually
    - *Assessment of education, nutrition and emotional health needs:* No prior education, change in medication, A1c values, maintain health outcomes, planning pregnancy, support, weight issues, new life situations
  - ❸ Complicating factors occur
    - When new factors influence self-management: health and physical conditions, emotional factors, basic living needs
  - ❹ Transitions in care occur
    - At any point transitions occur: living situations, medical care team, insurance coverage and age-related changes

REFERENCES: Powers MA, et al. DSME/S Position Statement 2015. Diabetes Care, The Diabetes Educator, Journal of Academy of Nutrition and Dietetics.

DSME/S Algorithm of Care and Action Steps



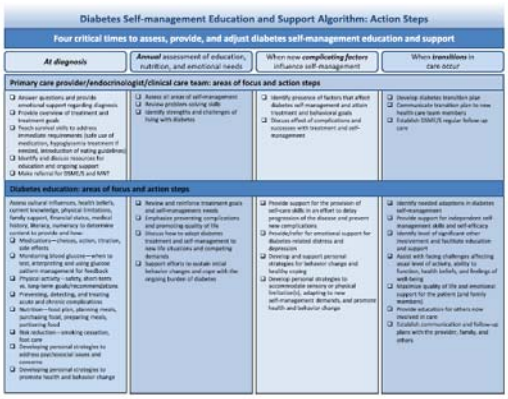
Diabetes Self-management Education and Support for Adults With Type 2 Diabetes: Algorithm of Care

ADA *Standards of Medical Care in Diabetes* recommends all patients be assessed and referred for:

Nutrition — Registered dietitian for medical nutrition therapy ⟺ Education — Diabetes self-management education and support ⟺ Emotional Health — Mental health professional, if needed

Four critical times to assess, provide, and adjust diabetes self-management education and support

1 *At diagnosis*	2 *Annual* assessment of education, nutrition, and emotional needs	3 When new *complicating factors* influence self-management	4 When *transitions* in care occur
When primary care provider or specialist should consider referral:			
❑ Newly diagnosed. All newly diagnosed individuals with type 2 diabetes should receive DSME/S ❑ Ensure that both nutrition and emotional health are appropriately addressed in education or make separate referrals	❑ Needs review of knowledge, skills, and behaviors ❑ Long-standing diabetes with limited prior education ❑ Change in medication, activity, or nutritional intake ❑ HbA$_{1c}$ out of target ❑ Maintain positive health outcomes ❑ Unexplained hyperglycemia or hypoglycemia ❑ Planning pregnancy or pregnant ❑ For support to attain and sustain behavior change(s) ❑ Weight or other nutrition concerns ❑ New life situations and competing demands	Change in: ❑ Health conditions such as renal disease and stroke, need for steroid or complicated medication regimen ❑ Physical limitations such as visual impairment, dexterity issues, movement restrictions ❑ Emotional factors such as anxiety and clinical depression ❑ Basic living needs such as access to food, financial limitations	Change in: ❑ Living situation such as inpatient or outpatient rehabilitation or now living alone ❑ Medical care team ❑ Insurance coverage that results in treatment change ❑ Age-related changes affecting cognition, self-care, etc.



Diabetes Self-management Education and Support Algorithm: Action Steps

Four critical times to assess, provide, and adjust diabetes self-management education and support

At diagnosis	*Annual* assessment of education, nutrition, and emotional needs	When new *complicating factors* influence self-management	When *transitions* in care occur
Primary care provider/endocrinologist/clinical care team: areas of focus and action steps			
❑ Answer questions and provide emotional support regarding diagnosis ❑ Provide overview of treatment and treatment goals ❑ Teach survival skills to address immediate requirements (safe use of medications, hypoglycemia treatment if needed, introduction of eating guidelines) ❑ Identify and discuss resources for education and ongoing support ❑ Make referral for DSME/S and MNT	❑ Assess all areas of self-management ❑ Review problem-solving skills ❑ Identify strengths and challenges of living with diabetes	❑ Identify presence of factors that affect diabetes self-management and attain treatment and behavioral goals ❑ Discuss effect of complications and successes with treatment and self-management	❑ Develop diabetes transition plan ❑ Communicate transition plan to new health-care team members ❑ Establish DSME/S regular follow-up care
Diabetes education: areas of focus and action steps			
Assess cultural influences, health beliefs, current knowledge, physical limitations, family support, financial status, medical history, literacy, numeracy to determine content to provide and how: ❑ Medication—phenols, acides, titration, side effects ❑ Monitoring blood glucose—when to test, interpreting and using glucose pattern management for feedback ❑ Physical activity—safety, short-term vs. long-term goals/recommendations ❑ Preventing, detecting, and treating acute and chronic complications ❑ Nutrition—food plan, planning meals, purchasing food, preparing meals, portioning food ❑ Risk reduction—smoking cessation, foot care ❑ Developing personal strategies to address psychosocial issues and concerns ❑ Developing personal strategies to promote health and behavior change	❑ Review and reinforce treatment goals and self-management needs ❑ Emphasize preventing complications and promoting quality of life ❑ Discuss how to adapt diabetes treatment and self-management to new life situations and competing demands ❑ Support efforts to sustain initial behavior changes and cope with the ongoing burden of diabetes	❑ Provide support for the provision of self-care skills in an effort to delay progression of the disease and prevent new complications ❑ Provide/refer for emotional support for diabetes-related distress and depression ❑ Develop and support personal strategies for behavior change and healthy coping ❑ Develop personal strategies to accommodate sensory or physical limitation(s), adapting to new self-management demands, and promote health and behavior change	❑ Identify needed adaptions in diabetes self-management ❑ Provide support for independent self-management skills and self-efficacy ❑ Identify level of significant other involvement and facilitate education and support ❑ Assist with facing challenges affecting usual level of activity, ability to function, health beliefs, and feelings of well-being ❑ Maximize quality of life and emotional support for the patient (and family members) ❑ Provide education for others now involved in care ❑ Establish communication and follow-up plans with the provider, family, and others

REFERENCES: Powers MA, et al. DSME/S Position Statement 2015. Diabetes Care, The Diabetes Educator, Journal of Academy of Nutrition and Dietetics.

Diabetes Self-management Education and Support for Adults With Type 2 Diabetes: Algorithm of Care

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Nutrition
Registered dietitian for medical nutrition therapy

⟺

Education
Diabetes self-management education and support

⟺

Emotional Health
Mental health professional, if needed

Four critical times to assess, provide, and adjust diabetes self-management education and support

1	2	3	4
At diagnosis	***Annual*** assessment of education, nutrition, and emotional needs	When new ***complicating factors*** influence self-management	When ***transitions*** in care occur
When primary care provider or specialist should consider referral:			
❑ Newly diagnosed. All newly diagnosed individuals with type 2 diabetes should receive DSME/S ❑ Ensure that both nutrition and emotional health are appropriately addressed in education or make separate referrals	❑ Needs review of knowledge, skills, and behaviors ❑ Long-standing diabetes with limited prior education ❑ Change in medication, activity, or nutritional intake ❑ HbA_{1c} out of target ❑ Maintain positive health outcomes ❑ Unexplained hypoglycemia or hyperglycemia ❑ Planning pregnancy or pregnant ❑ For support to attain and sustain behavior change(s) ❑ Weight or other nutrition concerns ❑ New life situations and competing demands	Change in: ❑ Health conditions such as renal disease and stroke, need for steroid or complicated medication regimen ❑ Physical limitations such as visual impairment, dexterity issues, movement restrictions ❑ Emotional factors such as anxiety and clinical depression ❑ Basic living needs such as access to food, financial limitations	Change in: ❑ Living situation such as inpatient or outpatient rehabilitation or now living alone ❑ Medical care team ❑ Insurance coverage that results in treatment change ❑ Age-related changes affecting cognition, self-care, etc.

REFERENCES: Powers MA, et al. DSME/S Position Statement 2015. Diabetes Care, The Diabetes Educator, Journal of Academy of Nutrition and Dietetics.

Diabetes Self-management Education and Support Algorithm: Action Steps

Four critical times to assess, provide, and adjust diabetes self-management education and support

Primary care provider/ endocrinologist/ clinical care team: area of focus and action steps

At diagnosis	***Annual*** assessment of education, nutrition, and emotional needs	When new ***complicating factors*** influence self-management	When ***transitions*** in care occur
❑ Answer questions and provide emotional support regarding diagnosis ❑ Provide overview of treatment and treatment goals ❑ Teach survival skills to address immediate requirements (safe use of medication, hypoglycemia treatment if needed, introduction of eating guidelines) ❑ Identify and discuss resources for education and ongoing support ❑ Make referral for DSME/S and MNT	❑ Assess all areas of self-management ❑ Review problem-solving skills ❑ Identify strengths and challenges of living with diabetes	❑ Identify presence of factors that affect diabetes self-management and attain treatment and behavioral goals ❑ Discuss effect of complications and successes with treatment and self-management	❑ Develop diabetes transition plan ❑ Communicate transition plan to new health care team members ❑ Establish DSME/S regular follow-up care

Diabetes Education: areas of focus and action steps

Assess cultural influences, health beliefs, current knowledge, physical limitations, family support, financial status, medical history, literacy, numeracy to determine content to provide and how: ❑ Medications—choices, action, titration, side effects ❑ Monitoring blood glucose—when to test, interpreting and using glucose pattern management for feedback ❑ Physical activity—safety, short-term vs. long-term goals/recommendations ❑ Preventing, detecting, and treating acute and chronic complications ❑ Nutrition—food plan, planning meals, purchasing food, preparing meals, portioning food ❑ Risk reduction—smoking cessation, foot care ❑ Developing personal strategies to address psychosocial issues and concerns ❑ Developing personal strategies to promote health and behavior change	❑ Review and reinforce treatment goals and self-management needs ❑ Emphasize preventing complications and promoting quality of life ❑ Discuss how to adapt diabetes treatment and self-management to new life situations and competing demands ❑ Support efforts to sustain initial behavior changes and cope with the ongoing burden of diabetes	❑ Provide support for the provision of self-care skills in an effort to delay progression of the disease and prevent new complications ❑ Provide/refer for emotional support for diabetes-related distress and depression ❑ Develop and support personal strategies for behavior change and healthy coping ❑ Develop personal strategies to accommodate sensory or physical limitation(s), adapting to new self-management demands, and promote health and behavior change	❑ Identify needed adaptions in diabetes self-management ❑ Provide support for independent self-management skills and self-efficacy ❑ Identify level of significant other involvement and facilitate education and support ❑ Assist with facing challenges affecting usual level of activity, ability to function, health beliefs, and feelings of well-being ❑ Maximize quality of life and emotional support for the patient (and family members) ❑ Provide education for others now involved in care ❑ Establish communication and follow-up plans with the provider, family, and others

REFERENCES: Powers MA, et al. DSME/S Position Statement 2015. Diabetes Care, The Diabetes Educator, Journal of Academy of Nutrition and Dietetics.

Hot topics

Sweeteners

Low calorie sweeteners and health

Marketing Madness

"net carbs", fiber consumption and source

Cooking Oils

What's the difference or what is preferred?

REFERENCES: Please indicate journal name, year, issue/volume, pages (Keep in font size 8)

Low & Reduced Calorie Sweeteners & Health

- Acceptable Daily Intake (ADI) is established as the amount of an ingredient, expressed on a body weight basis, that can be taken DAILY in the diet OVER A LIFETIME without risk
- The ADI is a conservative estimate: Generally a 100-fold safety level above that which produces not adverse effects (NOAEL)

REFERENCES: Academy of Nutrition & Dietetics Position Paper. Use of Nutritive and Nonnutritive Sweeteners. J Acad Nutr Diet. 2012.112(5):739-758.
Nonnutritive Sweeteners: Current Use and Health Perspectives: A Scientific Statement from the American Diabetes and the American Heart Association. Diabetes Care.

Low and Reduced Calorie Sweeteners: ADI

SWEETENERS	ADI	ADI EQUIVALENT (approx.)
Aspartame	50 mg	18-12 oz. cans diet soda, OR 100 Equal packets
Acesulfame K	15 mg	Typically not used as stand alone sweetener, but in blends
Sucralose	5 mg	30 Splenda packets, OR 5-12 oz. cans soda sweetened 100% w sucralose
Rebiana A	12 mg	5-12 oz. soda; approx. 24 packets

REFERENCES: www.fda.gov; accessed Sept 20. 2016

Low & Reduced Calorie Sweeteners: Controversies

- Do LCS cause people to compensate for the calories that they are saving?
- Do LCS increase food intake?
- Do LCS increase appetite, hunger, or induce cravings for sweets?
- Can LCS help people maintain or lose weight?
- Do LCS cause people to gain weight?

- LCS = Low calorie sweetener(s)

REFERENCES: Commission on Dietetic Registration Webinar. Research Update: What's New with Low Calorie Sweeteners. April 28, 2015.

Recommendations from Organizations:

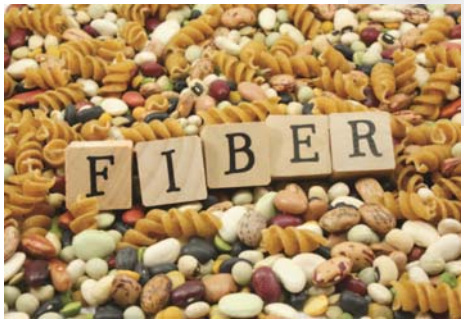
- Position of Academy of Nutrition & Dietetics 2012
- American Diabetes Association/American Heart Association Scientific Statement 2014
- American Diabetes Association Nutrition Therapy Recommendations for Management of Adults with Diabetes 2014
- American Cancer Society/National Cancer Institute 2015
- Academy of Nutrition & Dietetics Evidence Analysis Library 2012

Sweetener Summary

- All FDA approved low calorie sweeteners are safe for consumption
- Low calorie sweeteners provide a sweet taste with few or no calories
- Denial of sweet foods may increase their attractiveness and subsequent overeating
- Balance, variety and moderation are the keys to a healthy diet and healthy lifestyle
- LCS are not a magic bullet for weight loss; they are one tool within a comprehensive plan
- If used judiciously, LCS benefit weight loss/control and other metabolic parameters

REFERENCES: Academy of Nutrition and Dietetics. Use of nutritive and nonnutritive sweeteners (position paper.) J Acad Nutr Diet 2012; 112(5):739-757.

Marketing Madness: Net Carbs



WHAT ARE NET CARBS?

- Term invented by food industry to attract consumers and proponents of "low carb" food fad
- Term "net carbs" has no legal definition; is not used by FDA or the American Diabetes Association or Academy of Nutrition and Dietetics
- If term "net carbs" appears on food label, read further
- If sugar alcohols > 5 grams, subtract half grams sugar alcohol from total carbohydrates, and count this as "available carbohydrate" for insulin adjustment purposes.
- Check fiber content. If insoluble fiber is listed under total carbs, subtract all of insoluble fiber from total carbs and from the total fiber grams.
  - *If fiber quantity is till > 5 grams/serving, subtract half dietary fiber grams from total carbohydrates, and use result as available carbs for insulin adjustment purposes.*

REFERENCE: Wheeler, M. Diabetes Forecast Dec 2014, www.diabetes.org Accessed Sept 26, 2016

Cooking Oils: What is the Truth?

- Healthful Fats: Encourage Patients to Choose More Often
  - *PUFA: nuts and seeds (walnuts, sunflower seeds, and ground flax seeds); fish (especially fatty fish such as salmon, mackerel, tuna, sardines, and herring); and sunflower, safflower, soybean, corn, and canola oils*
  - *MUFA: avocados, nuts (almonds, hazelnuts, and pecans) and seeds (pumpkin & sesame); peanut butter and other nut butters; and olive, peanut, fallower, sunflower, and canola oils*
- Unhealthful Fats: Encourage Patients to Limit of Avoid)
  - *SFAs: butter, meats, coconuts; poultry with skin; high-fat dairy products (whole or 2% milk, cream, and ice cream); processed meats (ie, salami, bologna, sausage, ham, and bacon); and tropical oils (ie, coconut, palm kernel, or palm oil)*
  - *Trans fats: crackers, cookies, pastries, doughnuts, chips, stick margarines, and French fries*

REFERNCE: Diabetes Spectrum Nutrition FYI September 2016

Coconut Oil: What is the Truth?

- Coconut oil comes from dried coconut treated with chemicals to produce oil, often used in theatre popcorn, coffee creamer, and candy
- Touted as: helps burn fat, improve memory, improve heart health, prevent sunburn
- Contains 9 calories/gm and 120 calories/TB—just like canola and olive oil. Has unique flavor and texture, some prefer especially for baking
- Use only in moderation, like any other high fat cooking ingredient
- ½ cup coconut milk = 223 calories, 24 gm fat, 21 of which are saturated
- 1 cup coconut water = 46 calories, 0.5 gm fat 600 mg K, 252 mg Na; no evidence is any better hydrating agent than plain water
- Don't go cuckoo over coconut oil yet; think of it as condiment, not your daily "go-to" oil

REFERENCES: www.eatright.org; www.colostate.edu; www.naturaldatabase.therapeuticresearch.com

SUMMARY

- Medical nutrition therapy and diabetes self-management education and support are strongly correlated with improved clinical outcomes in diabetes care;
- Pharmacists are key players in delivery of nutrition education and diabetes self-management education and support, and making referrals to RDs for MNT as needed;
- The recent joint position paper on diabetes self-management education and support provides an excellent algorithm defining the what, when and how these services should be provided;
- Topics frequently asked about by clients with diabetes include sweeteners, net carbs, and the use of cooking oils

IPhA Annual Conference
Pre-conference Symposium
September 29, 2016

Advanced Clinical Management in Diabetes Care

Diabetes Medical Nutrition Therapy: The Role of the Pharmacist

Anne Daly, MS, RDN, BC-ADM, CDE
SIU School of Medicine Center for Family Medicine

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