Cases in Cost Effective Diabetes Management

Michael Humphrey, DO, Endocrinology
Michael Geishauser, PharmD, Clinical Pharmacist
UPMC Altoona Family Physicians

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Disclosures

- No conflicts of interest
- Any non FDA use of medications will be clearly identified

Goals

- What is the cost of diabetes mellitus?
- What are the goals of management?
- What represents EFFECTIVE management?
- What are the available options for management?
- How do we control costs?

EPIDEMIOLOGY OF diabetes 2012

- 29.1 million Americans = 9.3% of population
  - Diagnosed: 21.0 million
  - Undiagnosed: 8.1 million
- 1.5 million have type 1 diabetes
- Leading cause of kidney failure, non-traumatic LE amputation, blindness in adults
- Major cause of heart disease and stroke
- Seventh leading cause of death

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Nat. Diabetes Statistics 2014. niddk.nih.gov

Prediabetes

- Based on fasting blood sugar and HgA1C prediabetes detected in:
  - 37% of adults >20 years
  - 51% of adults >65 years
  - Estimated 86 million adults >20 years old

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Nat. Diabetes Statistics 2014. niddk.nih.gov

Economic cost of diabetes - 2017

- Total cost of diabetes: $327 billion
  - Direct costs 2/3, indirect costs 1/3
  - Increased by 26% over the last 5 years
  - Hospital inpatient 30%
  - Prescription medications for complications 30%
  - Anti-diabetic medications and supplies 15%
  - Physician office visits 13%
  - 2.3 x higher medical expenditure for patients with diabetes

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

American Diabetes Association. Diabetes Care; March 2018

Goals of Management

- Obtain/maintain patient happiness, functionality, productivity
- Obtain/maintain self-management skills
- Individualize goals
- Use team approach for above
- Cost control both short and long term
- Patient centered approach – emphasizing constructive interactions

Cost Effective management

- Glycemic Goals
  - HgA1C- 6.5 – 8.5%
  - SMBG's- pre meal 80-130, PP <180 mg/dl
  - CGM- periodic vs continuous
- Avoid hypoglycemia
  - Cost
  - Prevalence

Cost effective management

- Prevent microvascular complications
  - High cost in dollars and happiness
  - Requires long term optimal control
- HgA1C vs Time In Range (TIR)
  - Both are measures on long term control
  - TIR opens new measure of hour to hour variability

Cost effective management

- Prevent macrovascular events
  - Lifestyle
  - Blood pressure- optimal <130/80
  - Dyslipidemia- aggressive particle number lowering, Non HDL- <100
  - Hyperglycemia- HgA1C, TIR
  - Difficult to obtain the above trifecta!

Care Delivery Systems

- 33-49% of patients still do not meet targets for A1C, blood pressure, or lipids.
- 14% meet targets for all A1C, BP, lipids, and nonsmoking status.
- Progress in CVD risk factor control is slowing.
- Substantial system-level improvements are needed.
- Delivery system is fragmented, lacks clinical information capabilities, duplicates services & is poorly designed.

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

American Diabetes Association Standards of Medical Care in Diabetes. Promoting Health and Reducing Disparities in Populations. Diabetes Care 2017; 40 (Suppl. 1): S6-S10

Cost Effective Care

- Is low cost care ultimately cost effective when goals are not met and increased long term complications are the outcome?
- 2017 data- hospital inpatient care and retail prescriptions to treat complications were responsible for 60% of diabetes costs

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

American Diabetes Association. Diabetes Care, March 2018

Case 1

- 43 year old male presenting for yearly follow up. Voicing no complaints
- PMHx- hypertension, hyperlipidemia, overweight, tobacco use, ED
- FMHx- sister with T2DM, CAD in father
- PE- BP 138/82, BMI- 29 kg/m2
- Meds- atorvastatin 20 mg, amlodipine 5 mg, HCTZ 25 mg
- Labs- CBC, CC normal, TC-162, Tgl- 260, HDL- 32, A1C- 5.8%

Case 1

- What is his glycemic diagnosis?
- What is his estimated CVD risk?
- Would you intensify his lipid management?

Prediabetes and Type 2 Diabetes (1).

2.7 Screening for prediabetes and type 2 diabetes with an informal assessment of risk factors or validated tools should be considered in asymptomatic adults B

2.8 Testing for prediabetes and/or type 2 diabetes in asymptomatic people should be considered in adults of any age who are overweight or obese (BMI ≥25 kg/m^2 or ≥23 kg/m^2 in Asian Americans) and who have one or more additional risk factors for diabetes **(Table 2.3)** B

2.9 For all people, testing should begin at age 45 years B

2.10 If tests are normal, repeat testing carried out at a minimum of 3-year intervals is reasonable C

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Table 2.3—Criteria for testing for diabetes or prediabetes in asymptomatic adults

1. Testing should be considered in overweight or obese (BMI ≥25 kg/m^2 or ≥23 kg/m^2 in Asian Americans) adults who have one or more of the following risk factors:
   - First-degree relative with diabetes
   - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
   - History of CVD
   - Hypertension (≥140/90 mmHg or on therapy for hypertension)
   - HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
   - Women with polycystic ovary syndrome
   - Physical inactivity
   - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
2. Patients with prediabetes (A1C ≥5.7% [39 mmol/mol], IGT, or IFG) should be tested yearly.
3. Women who were diagnosed with GDM should have lifelong testing at least every 3 years.
4. For all other patients, testing should begin at age 45 years.
5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.

Underestimation of diabetes prevalence using HgA1C criteria- Endo 2019

- Sampled 9000 adults by HbA1C and 2 hr OGTT
- Values differed significantly, P <.000001
- Dx of DM by A1C criteria compared to OGTT was 26.92% sensitive and 99.39% specific
- A1C misclassified 73.07% of DM cases detected by OGTT, significantly underestimating true prevalence defined by OGTT

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Chung etal., 2019 Endocrine Society Annual Meeting

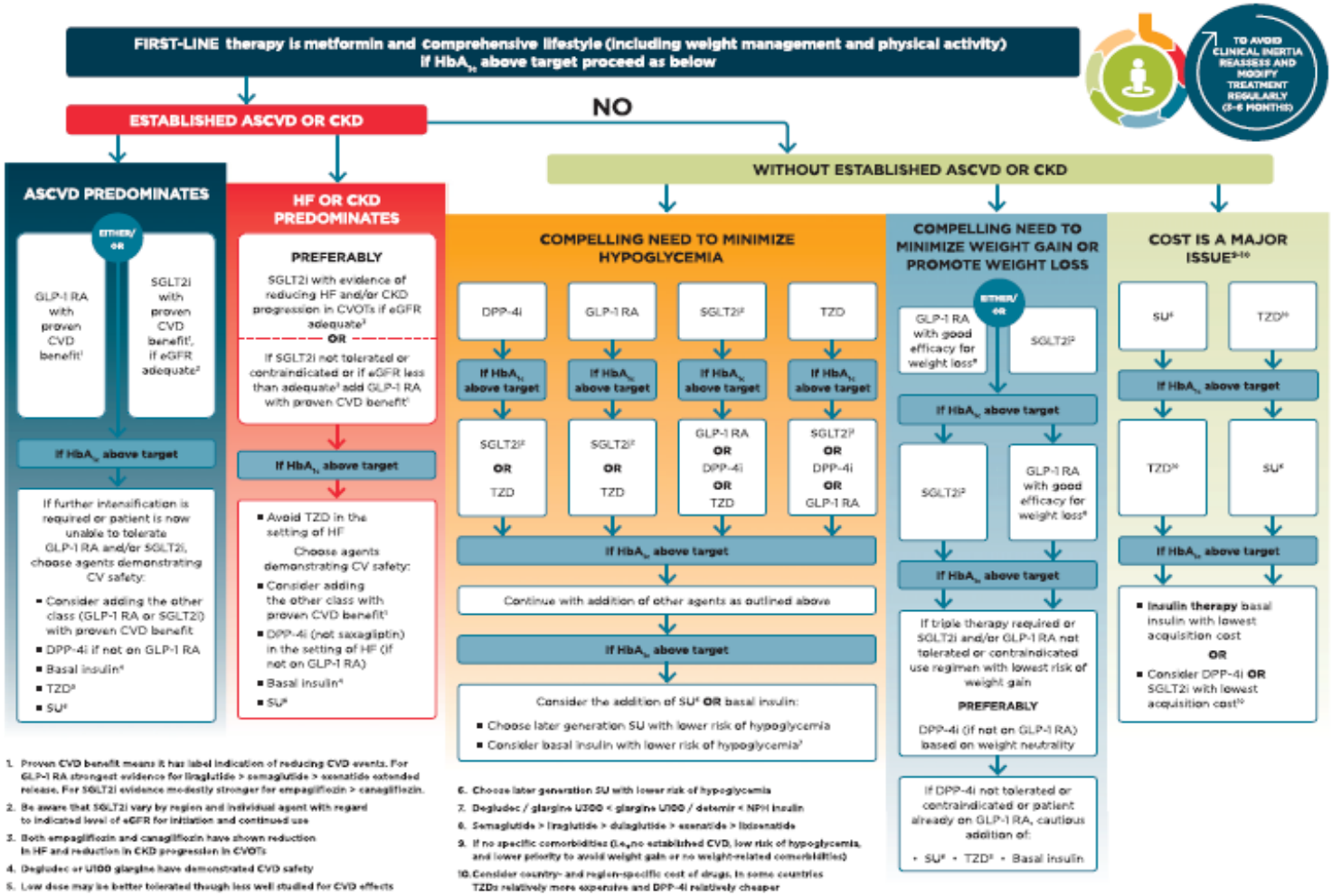
Case 1

- Estimated CVD risk over 10 years is 14.4% with lifetime risk of 69% using ASCVD plus risk calculator
- Intensification is indicated, LDL or Non-HDL and goal?
- Does have pre DM – lifestyle intervention +/- metformin (off-label)

Options for Management

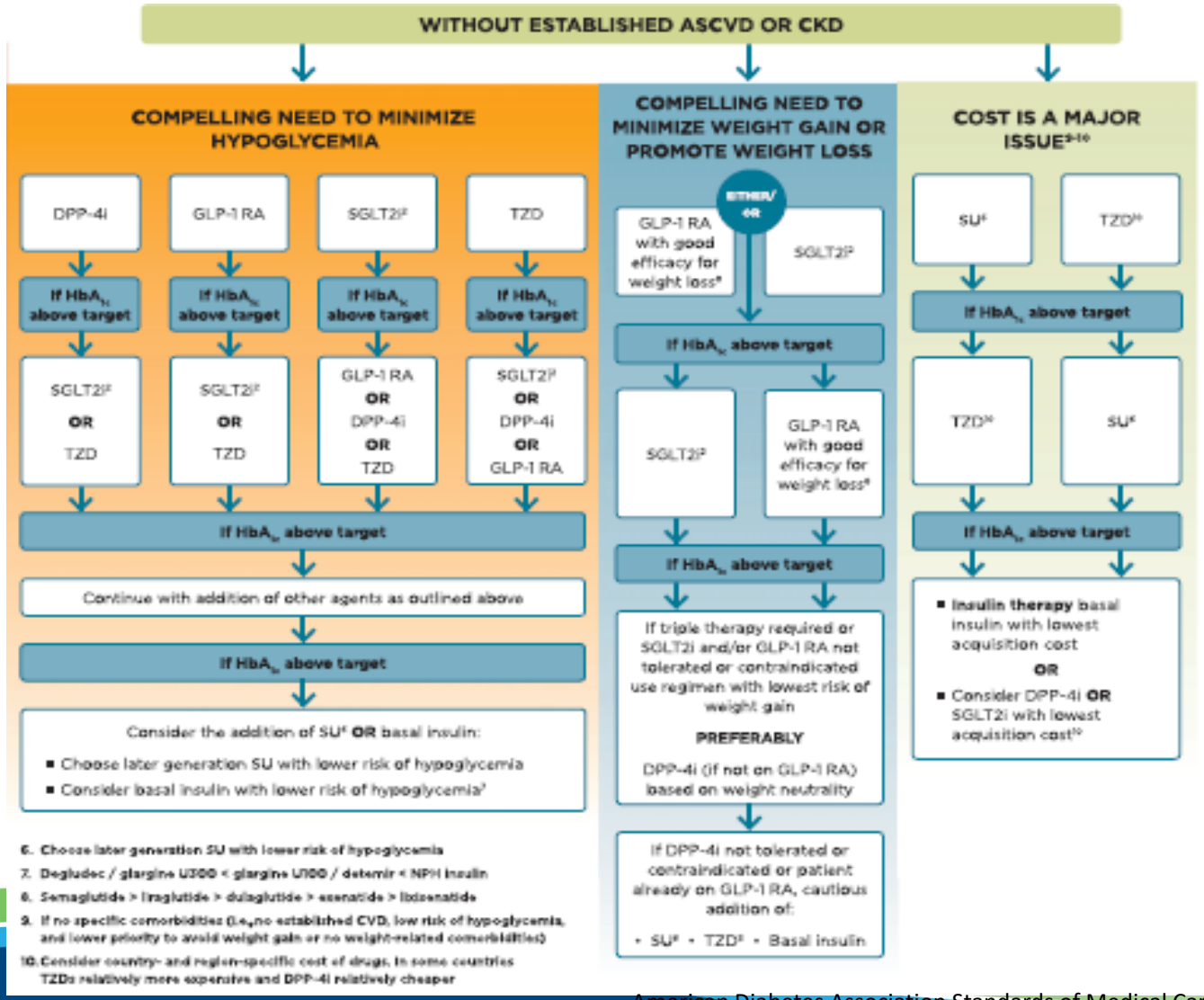
- GUIDELINES

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION



1. Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence for liraglutide > semaglutide > exenatide extended release. For SGLT2i evidence modestly stronger for empagliflozin > canagliflozin.
2. Be aware that SGLT2i vary by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Both empagliflozin and canagliflozin have shown reduction in HF and reduction in CKD progression in CVOTs
4. Degludec or U100 glargine have demonstrated CVD safety
5. Low dose may be better tolerated though less well studied for CVD effects
6. Choose later generation SU with lower risk of hypoglycemia
7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
9. If no specific comorbidities (i.e., no established CVD, low risk of hypoglycemia, and lower priority to avoid weight gain or no weight-related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

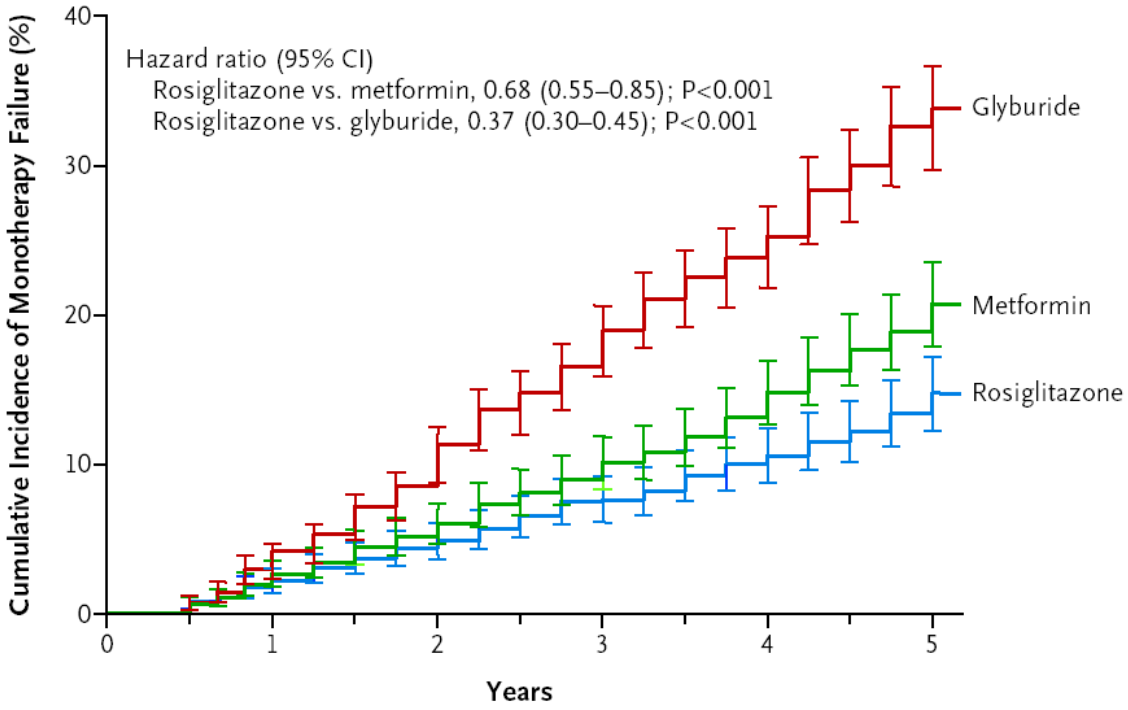
Figure 9.1—Glucose-lowering medication in type 2 diabetes: overall approach. For appropriate context, see **Fig. 4.1**. ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; CVOTs, cardiovascular outcomes trials; DPP-4i, dipeptidyl peptidase 4 inhibitor; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; SGLT2i, sodium–glucose cotransporter 2 inhibitor; SU, sulfonylurea; TZD, thiazolidinedione. Adapted from Davies et al. (39).



CADEMY OF
NS FOUNDATION

American Diabetes Association Standards of Medical Care in Diabetes.
Diabetes Care Volume 42, Supplement 1, January 2019

Kaplan-Meier Estimates of the Cumulative Incidence of Monotherapy Failure at 5 Years



No. at Risk

Rosiglitazone	1393	1207	1078	957	844	324
Metformin	1397	1205	1076	950	818	311
Glyburide	1337	1114	958	781	617	218

Kahn SE, et al. (ADOPT Study Group) N Engl J Med 2006;355:2427-43

Case 2

- 62 YO male with a history of T2DM (4 yr), dyslipidemia, overweight (BMI 29). Initiated on metformin 2000 mg daily at diagnosis with good response. Over the last one year A1C levels have been serially 5.8%, 6.2%, 6.4% in 3-4 month intervals.
- Other medications are atorvastatin 40 mg, losartan 50 mg BID, low dose aspirin
- He doses have problems with copay but is concerned his glycemic control is deteriorating. What additional actions would you consider?

CASE 2

- Sulfonylurea- low dose with caution for hypoglycemia
- Basal insulin such as NPH at HS if am hyperglycemia
- TZD- pioglitazone
  - This was started in 2012 at 15 mg bid with metformin 500 mg bid (*Actoplus Met*)
  - September 2019 HgA1C – 5.7%
  - However he has gained 30 #'s

Thiazolidinedione – TZD
Pioglitazone

- MOA- improves insulin sensitivity
  - Effective at hepatic, muscle and fat tissue
- Reduces HgA1C by 1 – 1.5%
- Improves pre and post prandial blood glucose levels

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Current Pharm. Design, 2009, 15:529-536

TZD – Pioglitazone
Non glycemic benefits

- Improve cholesterol/ dyslipidemia
- Improve blood pressure
- Improve NAFDL
- PCOS
- DM prevention
- Decrease risk of CVD, Stroke, death
- Preserves beta cell function

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Current Pharm. Design, 2009, 15:529-536

Pioglitazone Safety

- Hypoglycemia – low risk
- Weight gain – dose and time dependent. Fluid retention at higher doses.
- Heart Failure – with high fluid retention
- Skeletal fracture – decreased BMD/ increased fracture risk, particularly in women
  - ADOPT – fracture rate / 100 patient years
    - Rosi- 2.7, Metf. – 1.5, Glyb. – 1.3
  - PROactive – fracture rate
    - 5.1 vs 2.5% with placebo, only seen in females

Filipova, etal. Diab. Ther. 2017; 8(4);705. Lewis etal. JAMA 2015, 314(3):265-77

Pioglitazone safety

- Bladder Cancer – PROactive Study – 14 cases vs 5 in placebo
  - 10 yr observational study of pioglitazone – no increased risk
  - Metanalysis of 26 separate studies – no increased risk
- Hepatotoxicity – with troglitazone
  - Does not apply to rosiglitazone or pioglitazone
- Macular Edema – reported in prospective cohort study
  - ACCORD – eye subgroup 3473 patients found no link between TZD and DME

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Lewis etal. JAMA 2015, 314(3):265-77. Fong DS etal. Am J Ophth. 2009; 147(4);583

CASE 4

- You are seeing a 29 yo female diagnosed with DM at age 27. Started on metformin at dx and d/t inadequate control advance to insulin over the next 2 years. In Dec. 2018, using *Basaglar* 50 U QHS and lispro 15 U TID, ac meals.
- SMBG's – 200- 400+, A1C 04/2018 10.7%, now 14.5%

CASE 4

- DM ed and nutrition ed are UTD. Attempts to watch calorie/ carb intake
- Exercise- very limited d/t neuropathy and fibromyalgia
- PMHx- stage 3 obesity, fibromyalgia, HTN, dyslipidemia, childhood malignancy of AML

CASE 4

- Over the next 6 months, intensify lifestyle mx, add GLP-1 agent, titrate insulin regimen and on return in June current TDD of insulin is 208 units
- SMBGs remain 200-500 and A1C 14.5%
- Other then continuing to work on lifestyle, what would be your approach to this patient?

CASE 4

- Metabolic surgery?
- Initiated U-500 R and titrated over 4 months, continued GLP-1.
- Nov. 2019- feeling much better, SMBGs, 100-200 range, A1C 9.0%
- *Ozempic* increased to 1 mg weekly, continued U-500 titration

CASE 4

- CGM assessment
  - 11/15- 11/22, 2019
  - Avg BG- 135 mg/dl
  - GMI- 6.5%
  - SD- 25, CV- 14.4
  - TIR- 94%
  - TAR- 6%
  - TBR- 0%

CASE 4
Cost of Care

- U-100 Analogue insulin – $0.15 / unit (*GoodRx*) – 208 U/day = $11,232 /year
- U-500 R - $0.156 / unit – 80 U/day= $4,492 /year
- Semaglutide - $773 per 1.34 mg, metformin XR - $4 / 120 tablets (500 mg)
- HgA1C decreased from 14.5% to 9.0% (early Nov 2019)
- GMI to 6.5% on CGM with TIR of 94% and 0% TBR
- Feb 2018 – Oct 2019- 18 ED visits at $1389 = $25,000 / 7 Admission at $9850 = $68,950; 2017 Healthcare Cost and Utilization Project

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Addition of GLP-1, SGLT2, May Benefit Patients of U-500 Insulin

- Data on 17 pts, 8 GLP-1, 6 SGLT2, 3 both
- Initial mean: A1C: 8.6%, TDD 238, BMI 40.2, BW 120 kg
- After 3-6 months- A1C decreased to 7.6%, TDD to 205 units
- After 12 months- BMI 38 and BW to 113.8 Kg
- Reported a 29% increase in hypoglycemia

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Pardini etal. Annals of Pharm. June 2019

Using U-500 Insulin

- Use of concentrated insulin has increased over the past ten years due to the high incidence of insulin resistance and obesity in the population
  - The prevalence of obesity was 39.8% (93.3 million) of US adults in 2015 ~ 2016[1]
  - The diabetes rate in 2015 was 9.4% (30.3 million people) and another 84 million have pre-diabetes
  - Insulin resistance is the hallmark characteristic for type 2 diabetes mellitus

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

1. Adult Obesity Facts | Overweight & Obesity | CDC. Centers for Disease Control and Prevention. https://www.cdc.gov/obesity/data/adult.html. Accessed July 11, 2019.

Pharmacokinetics of U-500 Insulin

- Large doses of insulin require considerations about absorption
- Many factors influence insulin absorption after subcutaneous injection:
  - Site of injection
  - Dose of insulin
  - Depth of injection
  - Thickness of the subcutaneous fat layer
  - Exercise at the site
  - Temperature
  - Depth of injection

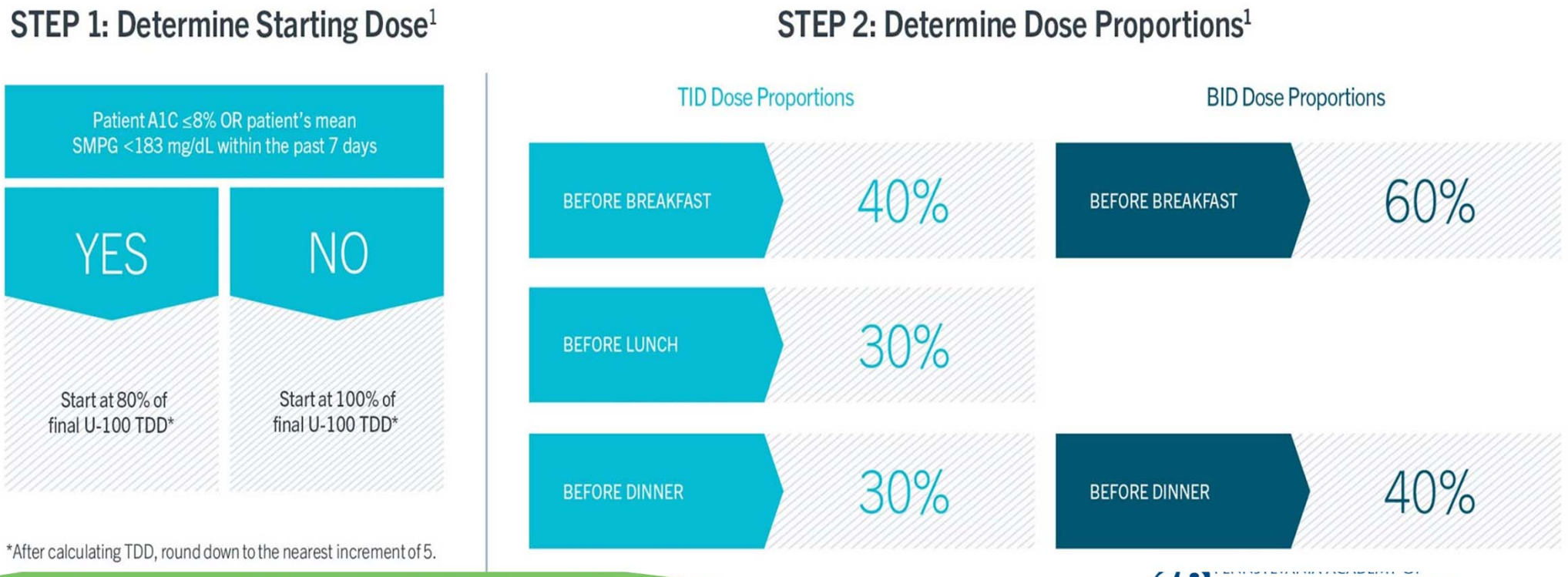
- **Volume is a key factor in absorption** due to surface area and diffusion
- It is more painful to inject larger volumes
  - There is a limit to the volume you can inject subcutaneously
    - Generally recognized as **around 1.5 mL**
  - The closer you are to the max, the more painful the injection
  - Decrease in patient adherence

- A smaller volume injected under the skin means better absorption and potentially better blood glucose control
- **Does U-500 have a different pharmacokinetic profile or does it work just like insulin regular U-100?**
  - The high concentration of U-500 makes the pharmacokinetic profile look very different from insulin regular U-100
  - **U-500 insulin has both prandial and basal characteristics**

U-100 vs. U-500			
Insulin	**Onset**	**Peak**	**Duration**
U-100	15-30 minutes	2.5-5 hours	4-12 hours
U-500	15-30 minutes	4-5 hours	13-24 hours

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Initiation of U-500 Insulin



FAMILY PHYSICIANS FOUNDATION

Hood RC, Arakaki RF, Wysham C, et al. Two treatment approaches for human regular U-500 insulin in patients with type 2 diabetes not achieving adequate glycemic control on high-dose U-100 insulin therapy with or without oral agents: a randomized, titration-to-target clinical trial. *Endocr Pract*. 2015;21(7):782-793. Erratum, 2016;22(7):905.

Treat-to-Target Dosing Algorithm With 2 or 3 Injections of U-500 Per Day

TID Initial Dose Proportions: 40:30:30[1]

INSULIN DOSE TO ADJUST	PLASMA-EQUIVALENT GLUCOSE VALUE*	SMPG (mg/dL)	DOSE TITRATION†
PRE-BREAKFAST	MEDIAN§ PRE-LUNCH SMPG	≤70‡	-10%
		71-130	No change in dose
PRE-LUNCH	MEDIAN§ PRE-DINNER SMPG	131-180	+5%
		181-220	+10%
PRE-DINNER	MEDIAN§ PRE-BREAKFAST SMPG	>220	+15%

BID Initial Dose Proportions: 60:40[1]

INSULIN DOSE TO ADJUST	PLASMA-EQUIVALENT GLUCOSE VALUE*	SMPG (mg/dL)	DOSE TITRATION†
		≤70‡	-10%
PRE-BREAKFAST	MEDIAN§ PRE-DINNER SMPG	71-130	No change in dose
		131-180	+5%
PRE-DINNER	MEDIAN§ PRE-BREAKFAST SMPG	181-220	+10%
		>220	+15%

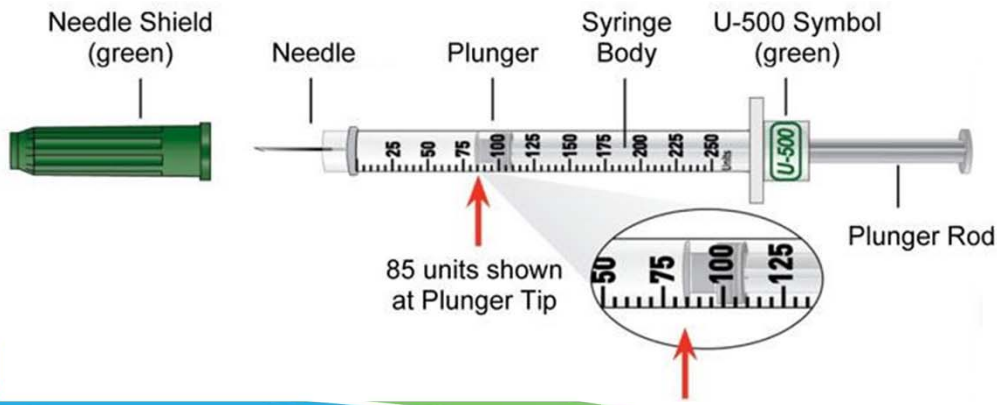
- † Used conventional rounding to nearest 5-unit increment
- ‡ 10% dose reduction if any pre-mealtime median, bedtime median, or single 3 AMSMPG ≤ 70 mg/dL

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

So Where Do the Errors Come From?

- The short answer: **SYRINGES**
- Prior to 2018, U-100 insulin syringes were the only type of insulin syringes on the market
- Traditionally, U-100 syringes, and sometimes TB syringes, were used to measure out U-500 doses

- Thankfully, specific U-500 syringes are available again
  - Available by prescription only **(U-100 syringes are technically OTC in PA)**
  - They have a **green cap** and can measure up to 250 units in 5 unit increments



https://diabetesed.net/wp-content/uploads/2016/10/u500-syringe.jpg

- Even easier is the availability of *Humulin R U-500 KwikPens*
- One box of two 3 mL *KwikPens* (3000 units/box) is approximately $600; whereas, one 20 mL vial (10,000 units/vial) of *Humulin R U-500* is approximately $1500
  - Vials are cheaper per unit, **but can increase the risk of error**

HUMULIN® R U-500 KwikPen®

insulin human injection U-500 (500 units/mL, 3 mL pen)

ADEMY OF
IS FOUNDATION

Case 5

- 54 yo executive with history of IDDM for 20 yrs. No micro./ macrovascular complications. Frequent hypoglycemia with poor awareness. SMBG >4 times daily with range <70 - >350 mg/dl. Reports severe hypoglycemia on at least 3 occasions in last 6 months at home and at work requiring EMS assistance. Current HgA1C 8.5%
- Regimen NPH 18 am, 12 pm late evening/ Reg- 0-6 units 2 hours post meals
- What are your recommendations on adjusting management of this patient?

Case 5

- Educate on hypoglycemia avoidance – eliminate severe lows, goal <1% below 70 mg/dl
- Update DSMES and nutrition on carbohydrate consumption/counting and pre meal dosing. Medical alert ID and glucagon use.
- Changed to MDI regimen with long acting/ short acting analogues
- Placed on real time CGM
- Notified Penn DOT
- Outcome good- improved control and eliminated severe hypoglycemia with CGM use

Managing IDDM patients

- Set specific goals for HgA1C and CGM
- Regimens include MDI or CSII (pump)
- Patient self-treatment skills/education are critical
- Nutritional management is critical
- CGM, preferable real time, offered to all patients willing to use

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Soupal etal. Glycemi results in IDDM with CGM. 2020 Diab. Care 43(1): 37-43

Prediabetic Conditions:

Benefit of Lifestyle Modification

Diabetes Prevention Program (DPP)

3,234 patients with elevated fasting and post-load glucose levels randomized to placebo, metformin (850 mg bid), or lifestyle modification* for 3 years

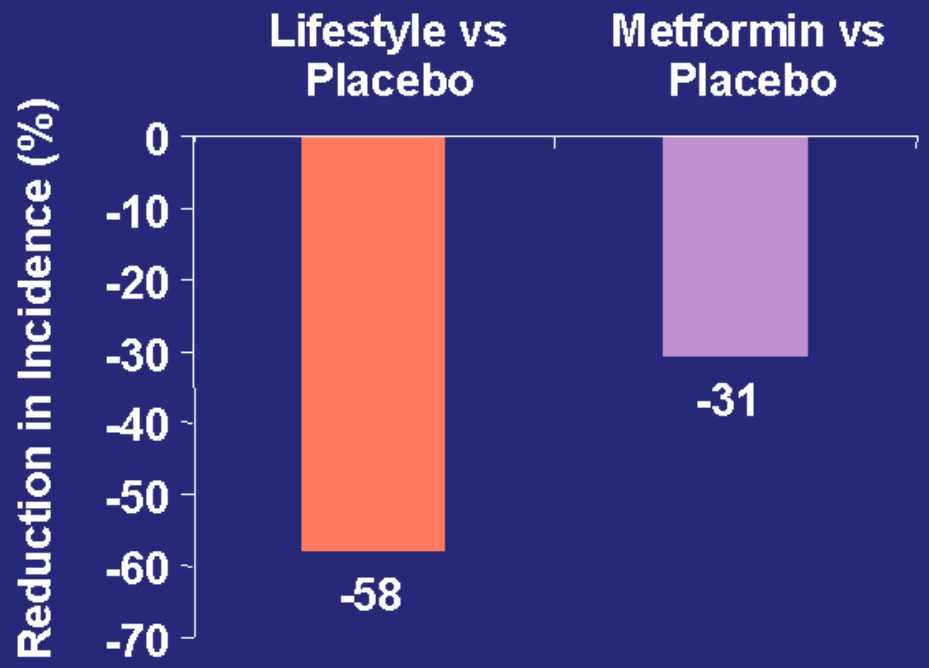
Lifestyle modification reduces the risk of developing DM

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

*Includes 7% weight loss and at least 150 minutes of physical activity per week

Knowler WC et al. *NEJM* 2002;346:393-403.

Diabetes Prevention Program: Reduction in Diabetes Incidence



N=3,234

39% lower incidence of diabetes in the lifestyle vs. metformin group

Diabetes Prevention Program Research Group. *N Engl J Med*. 2002;346:393-403.

LIFESTYLE

- How effective is lifestyle in prevention of T2DM and decreasing risk of complications?
- Zang, et al. Combined lifestyle factors and risk of incident T2DM and prognosis occurring in individuals with T2DM
  - Systemic review, 16 studies including 1,116,248 individuals by meta analysis
  - Investigated combined association of >/= 3 lifestyle factors for incident T2DM
  - Patients with healthiest class had 75% lower risk for T2DM vs least healthy, HR0.25, 95% CL 0.33-0.60)
  - Patients with T2DM and healthiest lifestyle had HR of 0.44- 0.51 for mortality/ CV disease

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Diabetologia. 10.1007, Sept 4, 2019

LIFESTYLE

- Gang, et al. Healthy Lifestyle with diabetes cuts CV disease risk
  - Studied individuals form Nurses' Health study 8,970, Health Prof. F/U Study 2,557, f/u 13.3 yrs
  - Lifestyle evaluation,1. high quality diet, 2. non smoking, 3. exercise >150 mins/week, 4. moderate EtOH
  - For participants with at least 3 low risk lifestyle factors
    - HR for total CVD incidence 0.48
    - HR for CAD incidence 0.53
    - HR for stroke incidence 0.33
    - HR for CVD mortality 0.32, $P<0.001$ for all end points

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

J Am Coll Card June 26, 2019

LIFESTYLE

- Gang, et al. conclusion
  - "These findings further support the tremendous benefits of adopting a healthy lifestyle in reducing the subsequent burden of cardiovascular complications in patients with type 2 diabetes."

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Gang, etal. Healthy lifestyle with diabetes cuts CV risk. J Am Coll. Card, June 2019

ADA Guidelines

- CVD Risk patient:
  - Metformin → GLP-1 agonist → SGLT2 → Basal insulin
- Cost Issues:
  - Metformin → Sulfonylurea/TZD → TZD/sulfonylurea → Cheapest basal insulin *or* DPP-4/SLGT2

Interpretation of CGM

- Name:
- DOB:
- Date of Study/Duration:
- Device:
- Recent lab HbA1c level:
- Average CGM Blood Glucose (mg/dl):
- Glucose Management Indicator(GMI):
- SD (10-26 mg/dl):
- CV (19-25%):
- Time in Range (TIR): > 70% goal
- Time above range (TAR):
- Time Below Range (TBR): < 4% goal with < 54 mg/dl at 0%
- Interpretation:
- Recommendation:

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Time In Range

- Assessing TIR association with microvascular complications
- Reviewed DCCT data for estimated TIR based on 7 point FSBG profiles for the 1,440 participants
- Findings: HR for development of retinopathy was increased by 64% and microalbuminuria outcome increased by 40%, for each 10 percentage points lower TIR, (Intensive gp 52% vs conventional 31% TIR)

- Validation of Time in Range as an Outcome Measure for Diabetes Clinical Trials. Beck et al. Diabetes Care 2019;42:400-405

Clinical Targets for Continuous Glucose Monitoring Data Interpretation

- Recommendations from the “International Consensus on Time in Range”
- Diabetes Care. August 2019. Volume 42,No 8:1593-1603.

Standardized CGM metrics for clinical care: 2019

- Number days CGM worn (recommend 14 days)
- Percent of time CGM is active (recommend 70% or data from 14 days)
- Mean glucose
- Glucose management indicator
- Glycemic variability (%CV) target <36%
- Time above range (TAR): % readings > 250 mg/dl, % > 181-250
- Time in range (TIR): % readings and time 70-180 mg/dl
- Time below range (TBR): % and time < 54-69, % < 54 mg/dl

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

CLinical Targets for CGM Data Interpretation. Diabetes Care. V42,N8. August 2019

CGM-Based Targets for IDDM and T2DM Populations

Target	IDDM and T2DM	High Risk IDDM/ T2DM
>250 mg/dl	<5%	<10%
>180 mg/dl	<25%	<50%
70-180 mg/dl	>70%	>50%
<70 mg/dl	<4%	<1%
<54 mg/dl	<1%	0%

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Battelino et al. Clinical Targets for CGM Interp. 2019 Diab. Care 42(8): 1593

CGM-Based Targets for IDDM and T2DM/GDM Pregnancy

Target	IDDM	T2DM/ GDM
>140 mg/dl	<25%	5%*
63-140 mg/dl	>70%	90%
<63 mg/dl	<4%	4%
<54 mg/dl	<1%	

*Targets for T2DM/ GDM not specified due to limited data

PENNSYLVANIA ACADEMY OF FAMILY PHYSICIANS FOUNDATION

Battelino etal. Clinical Targets for CGM Data Interp. 2019
Diab Care 42(8):1593

HbA1C vs CGM

- A1C
  - Current key surrogate marker for the development of long term diabetes complication in T1DM and T2DM
  - A1C reflects average glucose over the last 2-3 months
  - A1C is the only prospectively evaluated tool for assessing the risk for diabetes complications
  - A1C is important in clinical decision making

Limitation of HbA1C

- Lack of information about acute glycemic excursions and the acute complication of hypo- and hyperglycemia
- Fails to identify the magnitude and frequency of intra- and interday glucose variation
- A1C measures are confounded by anemia, iron deficiency, pregnancy, renal failure and can fail to accurately reflect mean glucose even when none of these conditions are present

Battelino, et al. Clinical Targets for CGM Monitoring Data Interpretation:. Diabetes Care, V42,N8:1593-1603.

CGM Benefits

- Allow for direct observation of glycemic excursions and daily profile which can inform on immediate therapy decisions
- Provides the ability to assess glucose variability and identify patterns of hypo- and hyperglycemia
- Effective use of CGM data requires the user to interpret the data and act upon them appropriately

CGM Drawbacks

- CGM data needs to be actively used in order to be effective
- May induce anxiety
- May have accuracy limitations, particularly with delay in registering blood glucose changes in dynamic situations
- Allergy at monitoring sites
- Not widely available in some regions

Battelino et al. Clinical Targets for CGM Monitoring. Diabetes Care. V42,N8: 1593-1603

Summary

- Diabetes mellitus – a common disease process resulting in a high social/ financial cost
- Management goals- delay onset (T2DM), = Lifestyle +/- metformin
- Diagnose early and treat aggressively, control BP, hyperglycemia and dyslipidemia
- Effective management requires that goals be met
- Cost control involves primarily avoiding admissions and preventing microvascular and macrovascular complications