




2017 CALTCM Annual Meeting

Quality Through Best Practices

April 28 & 29, 2017

CALTCM 2017 Quality Through Best Practices



43rd Annual Meeting
Quality Through Best Practices

California Association of Long Term Care Medicine
Promoting quality patient care through medical leadership and education

Challenges in Diabetes Management

Jane Weinreb, MD
Chief, Division of Endocrinology
VA Greater Los Angeles Healthcare System
Clinical Professor of Medicine
David Geffen School of Medicine at UCLA

CALTCM 2017

Speaker Disclosure Statement



Dr. Jane Weinreb has no relevant financial relationships with commercial interests to disclose.

CALTCM 2017

Quality Through Best Practices

Goals of Lecture



- Background
- Glycemic goals in older patients
 - How to individualize
 - Tips for how these can safely be achieved
- Define ways to minimize risk of hypoglycemia
 - Basic tenets to prevention, including reduction in use of sliding scale
 - Optimal management when hypoglycemia occurs
 - Drug regimens that reduce hypoglycemia risk
 - Use of newer technology and preparation for co-managing patients with insulin pumps.
- Glycemic management of obese patients with high insulin resistance

CALTCM 2017

Quality Through Best Practices

Classification of Diabetes



- **Type 1 DM:** due to autoimmune beta cell destruction, leading to absolute insulin deficiency. These patients need insulin for life.
- **Type 2 DM:** results from a progressive secretory defect on the background of insulin resistance. These patients often retain the ability to make insulin for many years.
 - 85-90% of diabetic adults.
 - Tend to be obese and may have other features of metabolic syndrome.
 - May need insulin (*can check a C-peptide to see if they make their own*)
- **Gestational DM:** diagnosed during the second or third trimester of pregnancy that is not clinically overt
- **Other specific types of DM:** due to other causes, including genetic defects in beta cell function or insulin action, diseases of the exocrine pancreas, drug or chemical induced.

Standards of Medical Care in Diabetes- 2017. American Diabetes Association. Diabetes Care 40(S1): S11-24, 2017.

CALTCM 2017

Quality Through Best Practices

Diabetes is Common in the LTC Setting



- Diabetes is an independent predictor of elderly placement in a LTC facility
- 26.8-34% prevalence in NH patients¹
- Cost of caring for diabetics in LTC facilities was **\$19.6 billion** in 2012²
- Important to review record for evidence of diabetes
 - On diabetes medication
 - Labs with hyperglycemia
 - Diabetes complications without prior diagnosis.

¹MN Munshi et al. Diabetes Care. 39:308-18, 2016.

²American Diabetes Association. Diabetes Care. 2013; 36:1033-46.

CALTCM 2017

Quality Through Best Practices

Presentation of Diabetes in Older Patients

<u>Metabolic Abnormality</u>	<u>Younger Patients</u>	<u>Older Patients</u>
Increased Osmolality	Polydipsia	Dehydration, Confusion, Delirium
Glycosuria	Polyuria	Incontinence
Insulin Deficiency	Polyphagia, Weight Loss	Anorexia, Weight Loss
Hypoglycemia	Sweating, palpitations	Headache, falls, MI, confusion, sleepy, slurred speech, bizarre behavior, seizures, coma

CALTCM 2017

Quality Through Best Practices

Glycemic Goals for Therapy

- The DCCT, VA Cooperative Study, and UKPDS provide convincing evidence that tight glycemic control results in delayed onset and slowed progression of microvascular complications.
- With each degree of improvement, there appears to be some benefit derived.
- The EDIC study reveals a ↓ in macrovasc events in type 1 diabetics with prior tight control. Similar confirmed in type 2 diabetics in the UKPDS follow up study.
- These studies include few patients >65 yrs of age.
- Takes several years to derive benefit.

DCCT, New Engl J Med, 329:977, 1993 VA Cooperative Study, Diabetes Care, 18:1113, 1995
 UKPDS, The Lancet, 352:837, 1998 Abaira et al. Diabetes Care. 21:574-9, 1998
 EDIC Study. N Engl J Med 2005; 353:2643-2653, 2005. Holman et al. N Engl J Med 359:1577-89, 2008

CALTCM 2017

Quality Through Best Practices

Tight Glycemic Control May Not ↓ Macrovascular Outcomes in Pts w/ CAD

- 3 trials done to assess CV benefit of tight glycemic control in patients with longstanding diabetes and either known CVD or high risk for such.
 - ACCORD Trial
 - ADVANCE Trial
 - VA Diabetes Trial
- Better microvascular outcomes in the tight control arm in all studies.
- No improved macrovascular outcome in any of the studies.
- Very low event rate in VADT, where all patients had impeccable BP and lipid control
- Increased deaths in the tight control arm of the ACCORD trial.
 - Especially in those with CAD or neuropathy.
 - Difficulty in achieving control.
- Perhaps once CV disease has developed, tight glycemic control may be more dangerous... Need to individualize glycemic control

The Accord Study Group. N Engl J Med;358:2545-59, 2008.
 The ADVANCE Collaborative Group. N Engl J Med;358:2560-72, 2008.
 Duckworth et al. N Engl J Med 360:129, 2009

CALTCM 2017

Quality Through Best Practices

Glycemic Goals for Older Adults

- Healthy older adults (good cognitive and physical function): appropriate to maintain aggressive goals and intensive therapy to:
 - lessen microvascular and macrovascular complications
 - minimize the effects on geriatric syndromes
 - improve quality and duration of life.
- Need to **individualize** goals based upon¹:
 - overall health status
 - level of function: aggressive control has not been shown to benefit older adults with low levels of function (3 or more limitations in IADL's or ADL's)²
 - personal and family desires.
- Need to take into consideration the time to expected benefit.
 - Life expectancy may be shorter than the time needed to benefit from the intervention
 - Microvascular benefits from tight glycemic control occur in ~few years
 - Benefit from BP and lipid control occurs in ~2-3 years.

¹Standards of Medical Care in Diabetes- 2017. Older Adults. American Diabetes Association. Diabetes Care 40(1): S99-104, 2017.

²Olson and Norris. Geriatrics 59:18-24, 2004

³American Geriatric Society Expert Panel on the Care of Older Adults with Diabetes Mellitus. JAGS. 61:2020-26, 2013.

CALTCM 2017

Quality Through Best Practices

ADA Glycemic Targets for Older Adults

Patient characteristics/ health status	Rationale	Reasonable A1C Goal	Fasting or Preprandial Glucose	Bedtime glucose
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy.	<7.5%	90-130 mg/dl	90-150 mg/dl
Complex/ Intermediate (multiple coexisting illnesses or 2+ instrumental ADL impairments or mild-to-moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk .	<8.0%	90-150 mg/dl	100-180 mg/dl
Very complex/ Poor health (LTC or endo-stage chronic illnesses or moderate-to-severe cognitive impairment or 2+ ADL dependencies)	Limited remaining life expectancy makes benefit uncertain. *Avoid hyperglycemia to prevent dehydration, electrolyte abnormalities, urinary incontinence, dizziness, falls, hyperglycemic crisis.	<8.5%	100-180 mg/dl	110-200 mg/dl

Standards of Medical Care in Diabetes- 2017. Older Adults. American Diabetes Association. Diabetes Care 40(S1): S101, 2017.
*Munshi et al, Diabetes Care. 39:308-18, 2016.

CALTCM 2017
Quality Through Best Practices

ADA Glycemic Targets for Older Adults

AGS guidelines recommend A1C goal be customized to burden of comorbidity, functional status, and life expectancy.


- Target A1C should generally be 7.5-8%
- May consider A1C of 7-7.5% in healthy older adults with few comorbidities and good functional status.
- May consider A1C of 8-9% for older adults with multiple comorbidities, poor health or limited life expectancy

American Geriatrics Society Expert Panel on the Care of Older Adults with Diabetes Mellitus. JAGS. 61:2020-26, 2013.

Standards of Medical Care in Diabetes- 2017. Older Adults. American Diabetes Association. Diabetes Care 40(S1): S101, 2017.
*Munshi et al, Diabetes Care. 39:308-18, 2016.

CALTCM 2017
Quality Through Best Practices






Case 1


- 85 y.o. man with h/o HTN, longstanding type 2 diabetes and dementia
- Tends to eat whatever he wants, whenever he wants
- On saxagliptin 2.5 mg, pioglitazone 30 mg
- Labs w/ eGFR 32, A1C 7.9%
- What is his A1C goal?
- How can we get there?

CALTCM 2017 Quality Through Best Practices



Approach to the Management of Hyperglycemia

Patient / Disease Features More stringent ← A1C 7% → Less stringent



The diagram illustrates the approach to managing hyperglycemia based on patient and disease features. It features a central scale from 'More stringent' to 'Less stringent' for an A1C target of 7%. The features and their corresponding positions on the scale are:

- Risks potentially associated with hypoglycemia and other drug adverse effects:** low (left) to high (right)
- Disease duration:** newly diagnosed (left) to long-standing (right)
- Life expectancy:** short (right)
- Relevant comorbidities:** severe (right)
- Established complications:** severe (right)
- Patient attitude and expected treatment efforts:** highly motivated, adherent, excellent self-care capabilities (left) to low motivated, non-adherent, poor self-care capabilities (right)
- Resources and support system:** readily available (left) to limited (right)


His A1C is about right

Usually not modifiable
Potentially modifiable

American Diabetes Association. Standards of Medical Care in Diabetes
2017. Glycemic Targets. Diabetes Care. 40(1):S53, 2017


CALTCM 2017 Quality Through Best Practices

Case 2



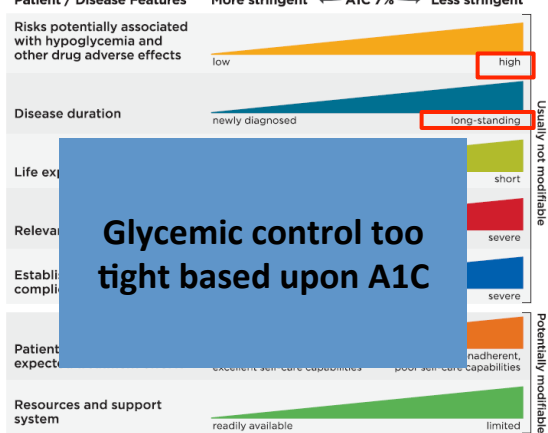
- 76 year old woman with longstanding Type 2 DM.
 - On metformin 1 gram BID AC, Glipizide 10 mg BID AC, Bedtime NPH insulin 34 units
 - Exam is benign including BMI of 25, weight 64 kg.
- FS BG reveals:
 - FBG's of 140-210 mg/dl
 - Prelunch, predinner, and prebed values of 80-135 mg/dl
- Labs reveal normal electrolytes, LFT's, and A1C 6.8%
- So, what do you think?

CALTCM 2017 Quality Through Best Practices



Approach to the Management of Hyperglycemia

Patient / Disease Features More stringent ← A1C 7% → Less stringent




Glycemic control too tight based upon A1C

American Diabetes Association. Standards of Medical Care in Diabetes-2017. Glycemic Targets. Diabetes Care. 40(1):S53, 2017.

CALTCM 2017Quality Through Best Practices

Case (cont'd)



- 3AM rings for help... “doesn’t feel well” ...
- So, what do you think?
- Nurse got a finger stick BG→BG 36 mg/dl, repeat 41 mg/dl
- Overnight symptoms are classic for hypoglycemia, as documented by her CBG’s.

CALTCM 2017Quality Through Best Practices

The Limiting Factor: Hypoglycemia

- Percent of patients >65 years old with one or more major hypoglycemic reaction:
 - Insulin 2.8% (up to 5% with NPH)
 - Sulfonylureas 1.2%
 - Metformin 0%
- Percent of patients with any hypoglycemic reaction:
 - Insulin up to 72% with NPH
 - Sulfonylureas 14%
 - Metformin 4%

CALTCM 2017

Quality Through Best Practices

Hypoglycemia in the Elderly

- Greatest risk for hypoglycemia:
 - Frail Elderly
 - Recent hospitalization within the past 30 days
 - The “oldest of the old”
 - Use of multiple medications
 - Renal and/or hepatic insufficiency
 - Elderly with dementia at higher risk of having a low.
- Counterregulatory responses are impaired in elderly diabetics
 - May have reduced warning symptoms (sweating, palpitations)
 - Dementia is a form of relative hypoglycemic unawareness

K Yaffe et al. Association between hypoglycemia and Dementia in a Biracial Cohort of Older Adults with Diabetes Mellitus. JAMA Intern Med. 2013; 173:1300-06.
ADA. Standards of Diabetes Care 2017: Glycemic Targets. Diabetes Care. 40(S1): S48-56, 2017.

CALTCM 2017

Quality Through Best Practices

Treatment of Hypoglycemia- Rule of 15



- When FS glucose is <70 mg/dl, give 15 grams carbohydrate
- Carbohydrate Sources (15-20 g) for Treating Hypoglycemia
 - ½ cup Fruit Juice
 - 1 cup Milk (no fat or low fat)
 - If unable to take p.o.'s, give glucose gel or glucagon and call MD
- Wait 15 minutes and recheck FS BG
 - If glucose is still <70 mg/dl, repeat 15 grams carb
 - Wait additional 15 minutes and recheck →If still low, repeat treatment and call MD
- Once SMBG returns to normal, the individual should consume a meal or snack to prevent recurrence of hypoglycemia.
- Inform physician of low so that regimen can be assessed and future low can be prevented.

A Core Curric for Diabetes Educators, 3rd Ed, AADE, Chicago, Illinois, 1998
 American Diabetes Association. Standards of Medical Care in Diabetes- 2017.
 Glycemic Targets. Diabetes Care. 40(S1):S53-4, 2017.

CALTCM 2017

Quality Through Best Practices

Prevention of nocturnal hypoglycemia



- Consider a bedtime snack, with increased carbohydrate and protein content if the BG<120 mg/dl
- Consider switch from:
 - Sulfonylurea to meglitinide (repaglinide, nateglinide) or a DPP-4 inhibitor (sitagliptin, saxagliptin, linagliptin, alogliptin)
 - Premeal regular insulin to a rapid acting analog (aspart, lispro, or glulisine)
- Move evening NPH to bedtime or change to glargine, detemir or degludec, preferably in the morning.
- Consider measurement of 3AM blood glucose once a week.

CALTCM 2017

Quality Through Best Practices

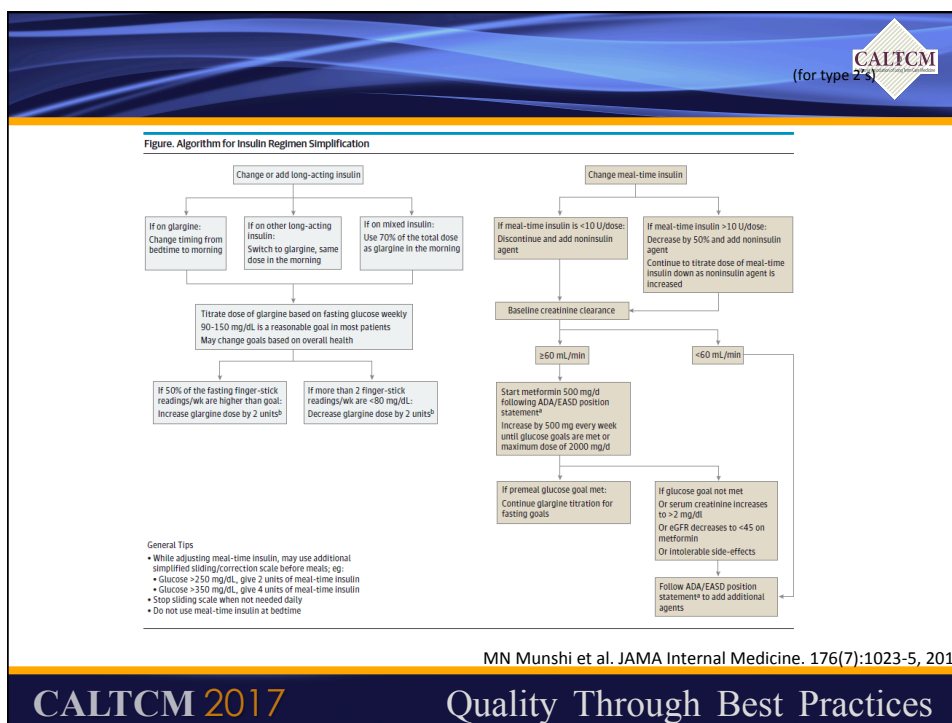
Simplify the regimen to get rid of lows

- Proof of concept study:
 - Single arm study of 65 patients ≥ 65 years old.
 - Diagnosed with T2DM based upon +C-peptide.
 - All patients were on ≥ 2 injections of insulin daily and had hypoglycemia.
 - Pts had mean age 76, mean diabetes duration 23 years, mean insulin injections per day 3.7.
- Able to improve A1C by $\sim 0.5\%$ with significant reduction in hypoglycemia.

MN Munshi et al. JAMA Internal Medicine. 176(7):1023-5, 2016

CALTCM 2017

Quality Through Best Practices



MN Munshi et al. JAMA Internal Medicine. 176(7):1023-5, 2016

CALTCM 2017

Quality Through Best Practices

Therapy: Medical Nutrition Therapy

- Diet and exercise remain the cornerstones of treatment, even in older patients
 - May consider weight reduction, if overweight
 - Should exercise including walking 30 mins 5x/wk and light weights
- Older patients with diabetes, especially in long term care facilities, tend to be underweight rather than overweight
 - Given the risk of undernutrition, **avoid food restrictions** in older individuals living in an institutionalized setting
 - Provide regular menus that are **consistent in carbohydrates and served at consistent times**.
- Use caution in prescribing caloric supplements, as these can be very high in carbohydrate.

CALTCM 2017

Quality Through Best Practices

Medical Therapy of Type 2 Diabetes- Aiming for low risk of lows


- First line drug therapy is always metformin as long as renal function is adequate
 - EGFR >60 ml/min can use full dose (1g BID AC)
 - EGFR 30-45 ml/min can use submax dose
 - EGFR <30 ml/min cannot use metformin
- If use long term, there is an increased risk of B12 deficiency, so should check B12 level and supplement as indicated.
- If additional therapy is warranted, choose in patient centered manner

ADA. Standards of Medical Care in Diabetes- 2017. Pharmacologic Approaches. Diabetes Care. 40(1):S64-74, 2017.
Kancherla et al. JAGS. 2017.

CALTCM 2017

Quality Through Best Practices

Agents with Low Risk of Hypoglycemia



Start with Monotherapy unless:

- A1C is greater than or equal to 9%, consider **Dual Therapy**.
- A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, consider **Combination Injectable Therapy** (See Figure 8.2).

Monotherapy	Metformin	Lifestyle Management
EFFICACY*	high	
HYPG RISK	low risk	
WEIGHT*	neutral/loss	
SIDE EFFECTS	GI/lactic acidosis	
COSTS*	low	

If A1C target not achieved after approximately 3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference = choice dependent on a variety of patient- & disease-specific factors).



Dual Therapy	Metformin +	Lifestyle Management																																				
	<table border="1"> <thead> <tr> <th>Sulfonylurea</th> <th>Thiazolidinedione</th> <th>DPP-4 inhibitor</th> <th>SGLT2 inhibitor</th> <th>GLP-1 receptor agonist</th> <th>Insulin (basal)</th> </tr> </thead> <tbody> <tr> <td>EFFICACY*</td> <td>high</td> <td>intermediate</td> <td>intermediate</td> <td>high</td> <td>highest</td> </tr> <tr> <td>HYPG RISK</td> <td>moderate risk</td> <td>low risk</td> <td>low risk</td> <td>low risk</td> <td>high risk</td> </tr> <tr> <td>WEIGHT*</td> <td>gain</td> <td>gain</td> <td>neutral</td> <td>loss</td> <td>gain</td> </tr> <tr> <td>SIDE EFFECTS</td> <td>hypoglycemia</td> <td>edema, HF, fxs</td> <td>rare</td> <td>GI, dehydration, fxs</td> <td>GI</td> </tr> <tr> <td>COSTS*</td> <td>low</td> <td>low</td> <td>high</td> <td>high</td> <td>high</td> </tr> </tbody> </table>	Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)	EFFICACY*	high	intermediate	intermediate	high	highest	HYPG RISK	moderate risk	low risk	low risk	low risk	high risk	WEIGHT*	gain	gain	neutral	loss	gain	SIDE EFFECTS	hypoglycemia	edema, HF, fxs	rare	GI, dehydration, fxs	GI	COSTS*	low	low	high	high	high	
Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)																																	
EFFICACY*	high	intermediate	intermediate	high	highest																																	
HYPG RISK	moderate risk	low risk	low risk	low risk	high risk																																	
WEIGHT*	gain	gain	neutral	loss	gain																																	
SIDE EFFECTS	hypoglycemia	edema, HF, fxs	rare	GI, dehydration, fxs	GI																																	
COSTS*	low	low	high	high	high																																	

If A1C target not achieved after approximately 3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference = choice dependent on a variety of patient- & disease-specific factors):


Triple Therapy	Metformin +	Lifestyle Management																																				
	<table border="1"> <thead> <tr> <th>Sulfonylurea +</th> <th>Thiazolidinedione +</th> <th>DPP-4 inhibitor +</th> <th>SGLT2 inhibitor +</th> <th>GLP-1 receptor agonist +</th> <th>Insulin (basal) +</th> </tr> </thead> <tbody> <tr> <td>T2D</td> <td>SU</td> <td>SU</td> <td>SU</td> <td>SU</td> <td>basal</td> </tr> <tr> <td>DPP-4-i</td> <td>DPP-4-i</td> <td>T2D</td> <td>T2D</td> <td>T2D</td> <td>DPP-4-i</td> </tr> <tr> <td>SGLT2-i</td> <td>SGLT2-i</td> <td>SGLT2-i</td> <td>DPP-4-i</td> <td>SGLT2-i</td> <td>SGLT2-i</td> </tr> <tr> <td>GLP-1-RA</td> <td>GLP-1-RA</td> <td>Insulin*</td> <td>GLP-1-RA</td> <td>Insulin*</td> <td>GLP-1-RA</td> </tr> <tr> <td>Insulin*</td> <td>Insulin*</td> <td>Insulin*</td> <td>Insulin*</td> <td>Insulin*</td> <td>Insulin*</td> </tr> </tbody> </table>	Sulfonylurea +	Thiazolidinedione +	DPP-4 inhibitor +	SGLT2 inhibitor +	GLP-1 receptor agonist +	Insulin (basal) +	T2D	SU	SU	SU	SU	basal	DPP-4-i	DPP-4-i	T2D	T2D	T2D	DPP-4-i	SGLT2-i	SGLT2-i	SGLT2-i	DPP-4-i	SGLT2-i	SGLT2-i	GLP-1-RA	GLP-1-RA	Insulin*	GLP-1-RA	Insulin*	GLP-1-RA	Insulin*	Insulin*	Insulin*	Insulin*	Insulin*	Insulin*	
Sulfonylurea +	Thiazolidinedione +	DPP-4 inhibitor +	SGLT2 inhibitor +	GLP-1 receptor agonist +	Insulin (basal) +																																	
T2D	SU	SU	SU	SU	basal																																	
DPP-4-i	DPP-4-i	T2D	T2D	T2D	DPP-4-i																																	
SGLT2-i	SGLT2-i	SGLT2-i	DPP-4-i	SGLT2-i	SGLT2-i																																	
GLP-1-RA	GLP-1-RA	Insulin*	GLP-1-RA	Insulin*	GLP-1-RA																																	
Insulin*	Insulin*	Insulin*	Insulin*	Insulin*	Insulin*																																	

If A1C target not achieved after approximately 3 months of triple therapy and patient (1) on oral combination, move to basal insulin or GLP-1-RA; (2) on GLP-1-RA, add basal insulin; or (3) on optimally stratified basal insulin, add GLP-1-RA or mealtime insulin. Metformin therapy should be maintained, while other oral agents may be discontinued on an individual basis to avoid unnecessarily complex or costly regimens (i.e., adding a fourth antihyperglycemic agent).

Combination Injectable Therapy (See Figure 8.2) http://professional.diabetes.org/sites/professional.diabetes.org/files/media/dc_40_s1_final.pdf






Med Rx of T2 DM- Other Oral Agents with Low Risk of Hypoglycemia



- **DPP-4 inhibitors (Sitagliptin, Saxagliptin, Linagliptin, Alogliptin)**
 - Prevents breakdown of intrinsic GLP-1 and GIP (our incretins), thereby increasing insulin secretion and suppressing glucagon secretion in a glucose dependent manner
 - Limited side effect profile, weight neutral
 - Can renally adjust dose, even in renal failure requiring dialysis.
 - Concerns: Increased risk pancreatitis, cost
- **SGLT2 inhibitors (Canagliflozin, Dapagliflozin, Empagliflozin)**
 - Block sodium glucose cotransporter in the proximal renal tubule, thereby enhancing excretion of glucose and sodium.
 - Must have adequate renal function (eGFR>45 ml/min).
 - Insulin independent means of action.
 - Enhances weight loss, reduces systolic and diastolic blood pressure.
 - Decreased mortality with 3.1 years empagliflozin.
 - Concerns: increased genital mycotic infections, UTI's, euglycemic DKA, cost.

ADA. Standards of Medical Care- 2017. Pharmacologic Approaches. Diabetes Care. 40(1):S64-74, 2017
 Inzucchi et al. Diabetes Care. 38:140-149, 2015; Zinman et al. New Engl J Med. 373:2117-28, 2015.
 Chon, Oxman, Mullur, Weinreb. Diabetes Medications in CKD. In: Endocrine Disorders in Kidney Disease. C
 Rhee and G Brent, Editors, In Press

Med Rx of T2 DM- Other Oral Agents with Low Risk of Hypoglycemia

- Alpha-Glucosidase Inhibitors (Acarbose, Miglitol)
 - Delay carbohydrate absorption via inhibition of intestinal poly and disaccharidases.
 - Decreases post-prandial glucose.
 - Concerns: significant GI side effects, need to take with every carb containing meal
- Thiazolidenediones (Pioglitazone, Rosiglitazone)
 - Move where fat is located, and thereby enhance peripheral insulin sensitivity, especially at muscle and adipose tissue
 - No reliance on renal excretion.
 - Concerns: weight gain, fluid retention with edema, decreased BMD, delayed onset of action.

Yang et al. Lancet Diabetes Endocrinol. 2:46-55, 2014

CALTCM 2017

Quality Through Best Practices

Med Rx of T2 DM- Other Oral Agents with Higher Risk of Hypoglycemia

- Sulfonylureas (Glipizide, Glyburide, Glimepiride)
 - Bind to specific receptors on the beta cells to promote insulin secretion in a non-glucose dependent manner
 - Inexpensive, but need to monitor BG which increases cost.
 - Concerns: significant hypoglycemia, especially in patients with impaired renal function or who skip meals, weight gain.
 - Avoid glyburide- active hepatic metabolites with increased risk of prolonged lows.
- Meglitinides: (Repaglinide, Nateglinide)
 - Bind to ATP-sensitive potassium channels on beta cells to increase insulin secretion in a non-glucose dependent manner
 - Rapid onset and offset permits better post-prandial control with fewer late lows.
 - Skip dose if skip meal, but need to take with every carb containing meal.
 - Repaglinide is hepatically metabolized- can use with renal insufficiency.
 - Concerns: hypoglycemia, frequent dosing schedule, weight gain, moderate cost.

CALTCM 2017

Quality Through Best Practices

Med Rx of T2DM- Injectable Therapies

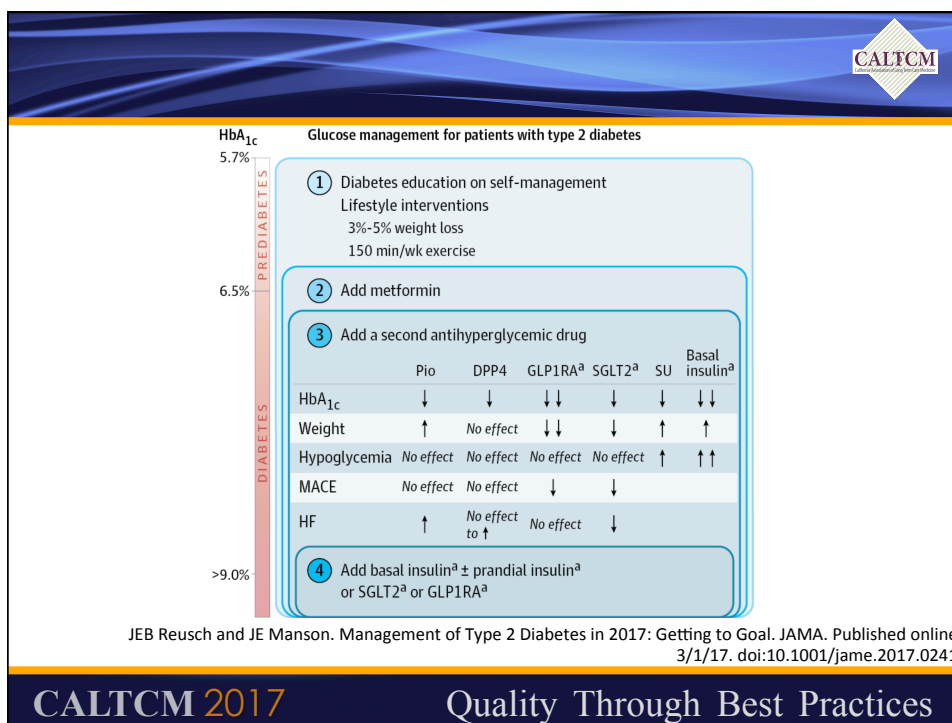
- GLP-1 Receptor Agonists (Exenatide, Liraglutide, Dulaglutide, Albiglutide)
 - Act like supraphysiologic levels incretins:
 - Enhance glucose stimulated insulin secretion and glucagon suppression
 - Slow gastric emptying and enhance satiety centrally
 - Low risk of hypoglycemia, weight loss, modest decrease in BP
 - Decreased mortality with 3.8 years lira
 - Concerns: increased risk of pancreatitis, significant GI side effects (nausea, vomiting, diarrhea), C-cell hyperplasia and MTC in rodents, cost.
- Basal insulins: (NPH, Glargine, Detemir, Degludec)
 - Activate insulin receptor to enhance postprandial glucose disposal and suppress hepatic glucose production.
 - Universally effective
 - Concerns: hypoglycemia, weight gain, training requirement, cost.



Marso et al. New Engl J Med. . 375:311-22, 2016

CALTCM 2017

Quality Through Best Practices



CALTCM 2017

Quality Through Best Practices

Why Not Just Use Sliding Scale Insulin?

- Dose is not individualized
- Insulin is reactive, rather than proactive
 - Giving insulin to cover when the BG is already high, rather than preventing the hyperglycemia



- Leads to wide fluctuations in glucose levels
- Does not provide basal insulinization (needed by insulin deficient diabetics) nor consider nutritional coverage

Leahy J. Endocr Pract 12:86-90, 2006
 Queale WS et al. Arch Intern Med 157:545-552, 1997
 Clement S et al. Diabetes Care 27:553-91, 2004
 American Diabetes Association. Diabetes Care 40(1):Supp, 2017

CALTCM 2017

Quality Through Best Practices

Why Not Just Use Sliding Scale Insulin?

The American Geriatrics Society strongly discourages use of insulin sliding scales in nursing home patients.

Use of sliding scale insulin has been noted to be associated with increased risk of hypoglycemia

Review of literature reveals that if supplemental scale is needed, the target should be no less than 200 mg/dl in order to avoid lows.

Leahy J. Endocr Pract 12:86-90, 2006
 Queale WS et al. Arch Intern Med 157:545-552, 1997
 Clement S et al. Diabetes Care 27:553-91, 2004
 American Diabetes Association. Diabetes Care 40(1):Supp, 2017

CALTCM 2017

Quality Through Best Practices

Case 3



- 68 y.o. woman with type 1 diabetes since age 18 presents for routine follow up.
- PMH: nonproliferative diabetic retinopathy
- Diabetes medication:
 - Glargine 8 units Q12 hours
 - Aspart 1 unit for every 10 grams carb, one extra unit for every 50 mg/dl over 150 mg/dl.
 - Switched to an insulin pump with aspart 1 year ago.
- Hypoglycemia still occurs ~2-4 times weekly, especially after exercise, but sometimes for no clear reason. Not improved despite higher glycemic targets and switch to pump therapy. Doesn't want to check her finger stick more often (already 4x/day)
- Exam: BMI 24 Appears well, remainder of exam unremarkable save for decreased sensation to monofilament on both feet.
- Labs: creatinine 0.76, eGFR 92 ml/min, A1C 8.2%
- Is there anything new that can help improve her glycemic control without increasing her risk of hypoglycemia?

CALTCM 2017

Quality Through Best Practices

Background



- Despite advancements in technology and therapeutics, only ~one third of people with type 1 diabetes achieve the level of glycemic control needed to avoid long-term complications.
- Additionally, tight glycemic control as well as insulin deficiency have been linked to an increased risk of hypoglycemia leading to morbidity as well as even mortality
- Finger stick BG monitoring, even when done multiple times each day, provides spotty data for diabetes management.

RW Beck, WV Tamborlane, RM Bergenstal et al. *J Clin Endocrinol Metab* 97:4383-9, 2012
 P Choudhary, SA Amiel. *Postgrad Med J* 87:298-306, 2011
 ER Seaquist, J Anderson, B Childs et al. *Diabetes Care* 36:1384-95, 2013

CALTCM 2017

Quality Through Best Practices

Background



- Despite advancements in technology and therapeutics, only ~one third of people with type 1 diabetes achieve the level of glycemic control needed to avoid long term complications
- Additional insulin increases morbidity as well as even mortality
- Fingerstick BG monitoring, even when done multiple times each day, provides spotty data for diabetes management.

RW Beck, WV Tamborlane, RM Bergenstal et al. *J Clin Endocrinol Metab* 97:4383-9, 2012
 P Choudhary, SA Amiel. *Postgrad Med J* 87:298-306, 2011
 ER Seaquist, J Anderson, B Childs et al. *Diabetes Care* 36:1384-95, 2013

CALTCM 2017

Quality Through Best Practices

Insulin Pumps: Terminology



- Basal rate: units of insulin infused per hour
 - Predetermined by physician
 - Can have different basal rates throughout the day
 - Can set a temporary basal rate for exercise
- Bolus dose: amount of insulin infused over a short period
 - Most modern pumps use a bolus calculator based upon planned carbohydrate intake, blood glucose, and “insulin on board”
- Reservoir: amount of insulin each pump can hold
- Infusion Set: tubing and skin insertion site where pump cannula attaches to the body.



CALTCM 2017

Quality Through Best Practices

Minimed 670G: A hybrid closed-loop insulin delivery system



- FDA has approved a hybrid closed-loop insulin delivery system for use in patients ≥ 14 years old with type 1 diabetes.
- System uses a "smart algorithm" that "learns an individual's insulin needs" to permit it to automatically adjust basal insulin doses based on readings from a continuous glucose monitor (CGM).
 - Basal insulin is delivered in fully "auto" mode.
 - Mealtime boluses need to be delivered by the patient.
- Also has an automated "suspend before low" feature that alerts the patient and stops insulin delivery for up to 2 hours when the glucose reading approaches a prespecified low level.
- Expect it to be available Spring 2017.



Med Lett Drugs Ther 2016

CALTCM 2017

Quality Through Best Practices

Safety of a Hybrid Closed-Loop Insulin Delivery System in Patients with Type 1 Diabetes



- 124 type 1 diabetics in a single arm trial.
 - ages 14-75 (mean age 37.8 years)
 - mean duration of disease 21.7 years
 - mean total daily insulin dose 47.5 units
 - On insulin pump therapy for at least 6 months
- After a two week run-in period, patients entered a 3 month at home study period.
- Outcomes were:
 - Percent of glucose values in target range
 - Hypoglycemia, diabetic ketoacidosis, and hyperglycemia (BG > 300 mg/dl [16.6 mmol/L])

CALTCM 2017

Quality Through Best Practices

Safety of a Hybrid Closed-Loop Insulin Delivery System in Patients with Type 1 Diabetes




Table 2. Glucose Control, Insulin Usage, and Weight Among Patients Using Hybrid Closed-Loop Systems

Parameter	Run-in Period	Study Period
Sensor glucose, mean (SD) [median], mg/dL	150.2 (22.7) [150.1]	150.8 (13.7) [149.9]
Percentage of time with glucose level in range, mean (SD); median (IQR)		
Sensor glucose values		
>300 mg/dL	2.3 (1.2); 0.2 (0.2-2.6)	1.7 (1.9); 0.0 (0.5-2.1)
>180 mg/dL	27.4 (13.7); 26.7 (16.0-37.2)	24.5 (9.2); 24.1 (17.3-29.8)
71-180 mg/dL	66.7 (12.2); 67.5 (59.0-75.1)	72.2 (8.8); 73.0 (67.7-78.4)
≤70 mg/dL	5.9 (4.1); 5.4 (2.0-6)	3.3 (2.0); 2.8 (1.7-4.3)
≤50 mg/dL	1.0 (1); 0.6 (0.2-1.3)	0.6 (0.6); 0.4 (0.2-0.8)
Sensor glucose values at night time only ^a		
>180 mg/dL	26.8 (15.2); 26.7 (15.3-35.8)	21.0 (9.9); 20.9 (13.6-28.5)
71-180 mg/dL	66.8 (14.0); 67.8 (57.6-75.2)	75.3 (8.8); 76.4 (68.9-83.1)
≤70 mg/dL	6.4 (4.3); 6.2 (3.8-5)	3.1 (2.2); 3.0 (1.7-4.2)
Within-day SD of glucose, mean (SD); median (IQR), mg/dL ^b		
	50.1 (9.9); 48.9 (43.7-56.2)	46.7 (7.3); 45.6 (41.7-50.4)
Within-day coefficient of variation of glucose, mean (SD); median (IQR), %		
	33.5 (4.3); 33.1 (30.3-36.4)	30.8 (3.3); 30.7 (28.2-33.0)
Glycated hemoglobin, mean (SD) [median], %	7.4 (0.9) [7.3]	6.9 (0.6) [6.8]
Total daily dose of insulin, mean (SD) [median], U	47.5 (22.7) [43.9]	50.9 (26.7) [44.1]
Weight, mean (SD) [median], kg	76.9 (17.9) [73.5]	77.6 (16.1) [74.7]

Abbreviations: IQR, interquartile range.
 SI conversion factor: To convert glucose to mmol/L, multiply by 0.0555.
^a Night time was defined as 10:00 PM to 7:00 AM.
^b Measures of glycemic variability.


RM Bergenstal et al. JAMA 2016

CALTCM 2017


Quality Through Best Practices

- Less time hyper- or hypoglycemic, including overnight
- Improved A1C
- No severe hypoglycemic events or DKA
- Study limitations:
 - No control group
 - Included relatively healthy, well controlled patients
 - Short duration.

How about Continuous Glucose Monitors (CGM)?



- The Dexcom G5 Mobile Continuous Glucose Monitoring System has received FDA approval as a replacement for traditional fingerstick BG monitoring to determine insulin dosing
 - Composed of a sensor, a transmitter and a receiver or compatible mobile device.
 - Sensor measures interstitial glucose, and transmits glucose data and trend every five minutes.
 - MARD (mean absolute relative difference) in BG now 9%... Very similar to the MARD of glucose meters (5-9%).
- Still requires calibration with two daily fingersticks (at least Q12hrs)
- Due to its approval as a “therapeutic device”, the Centers for Medicare and Medicaid Services (CMS) has announced coverage of the Dexcom G5 mobile.



<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm534056.htm>
 Diabetes Technol Ther 18:512-16, 2016.

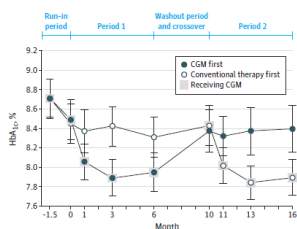
CALTCM 2017

Quality Through Best Practices

Use of CGM with Multiple Daily Injections (MDI) of Insulin



- Beck et al looked at 158 type 1 diabetics on MDI
 - A1C 7.5-9.9% (mean 8.6%), mean age 48, mean diabetes duration 19 years.
 - Randomized to CGM or usual care for 24 weeks.
 - Primary outcome change in A1C, secondary outcome hypoglycemia.
 - A1C decreased by 1% with MDI+CGM, 0.4% with just MDI
 - Duration of hypoglycemia <70 mg/dl was 43 min/d with MDI+CGM, 80 min/d with just MDI.
 - Bottom line: MDI+CGM had better glycemic control with fewer lows!



No. of patients
 CGM first: 69, 69, 69, 69, 69, 66, 67, 68, 69
 Conventional therapy first: 73, 72, 71, 73, 73, 73, 70, 73, 73

- Lind et al looked at 161 type 1 diabetics on MDI in an open-label crossover trial
 - A1C >7.5% (mean 8.6%), mean age 44, mean diabetes duration 22 years.
 - Each patient had 24 weeks of MDI+CGM and MDI alone, separated by a 17 week "wash out" period.
 - Mean A1C 7.92% w/ MDI+CGM, 8.35% w/ MDI alone (A1C difference 0.39%).

RW Beck, T Riddlesworth, K Ruedy et al. JAMA. 317:371-8, 2017.
 M Lind, W Polonsky, IB Hirsch et al. JAMA. 317:379-87, 2017.

CALTCM 2017

Quality Through Best Practices

Implications of New Diabetes Technology



- Hybrid closed loop insulin delivery system is another step towards an artificial pancreas → potential to improve glycemic control, decrease risk of severe lows, and perhaps improve quality of life.
- Continuous glucose monitoring improves QOL:
 - Reduces the need to check finger stick BGs multiple times a day
 - Helps to eliminate some of the disease-associated work and stress
 - Protects patients from hypoglycemia.

CALTCM 2017

Quality Through Best Practices

Case 4



- 72 y.o. gent with diabetes for 5 years and worsening glycemic control despite titration of insulin doses. Well controlled HTN, obesity, MS, otherwise well.
- Notes that he is constantly hungry and tries to snack on fruit throughout the day to be “healthy”
- Regimen: Metformin 1g BID AC, Glargine 80 units QPM, Aspart 30 TID AC.
- Exam reveals BMI 31, weight 100 kg
- Labs BGs 130’s-low 200’s over course of day, A1C is 8.6%.
- What is his A1C target?
- How can we get there?

CALTCM 2017

Quality Through Best Practices

Case 4



- Generally healthy, so would aim for tighter A1C (maybe <7.5%) if can get there without lows.
- High insulin doses (>1 unit/kg bw/day) may reflect severe insulin resistance (due to age, inactivity) or may reflect excess insulin use with resultant eating!
- Can try to cut insulin doses back to 1 unit per kg BW per day, or try to switch aspart to a GLP-1RA.

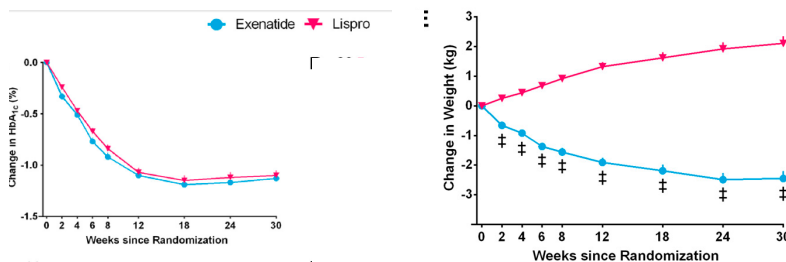
CALTCM 2017

Quality Through Best Practices

Basal Insulin plus GLP-1RA



- Diamant performed 30 week open label study of 627 patients not at A1C goal on glargine plus metformin.¹
 - Randomized to mealtime lispro or BID exenatide.
 - Fewer nocturnal lows with exenatide but more GI side effects.



- Meta-analysis revealed equal glycemic control with lower risk of hypoglycemia (0.67) and reduction in weight (-5.66 kg) compared with basal-prandial insulin therapy.²

¹Diamant et al. Diabetes Care 2014. 37:2483-90

²Eng et al. Lancet. 2014. 384:2228-34

CALTCM 2017

Quality Through Best Practices

Management of obese patients with severe insulin resistance



- Ensure no additional contributors to ↑'d resistance (unstable angina, infection, etc)
- Lifestyle needs to be stressed
 - Low carb snacks and reasonable carb portions in meals. Don't forget the protein!
 - Weight loss- even a little- helps a great deal
 - Exercise improves insulin sensitivity
 - Walking
 - Weights
- Ensure that they are not "overinsulinized"
 - Most patients with T2DM get adequate control with 1 unit/kg BW/day.
 - Consider cutting dose and observing if this improves BG's.
 - Check 2-3AM BG to ensure that they do not have nocturnal lows→ via Somogyi effect can get AM highs.
- Use antihyperglycemic medications that help with weight loss
 - GLP-1 receptor agonists decrease appetite.
 - SGLT2 inhibitors cause dumping of glucose in urine. (Can add a DPP-4 if need additional A1C lowering and don't want injections).
- Not a fan of concentrated insulins
- Gastric bypass very effective if health is okay.

CALTCM 2017

Quality Through Best Practices

Conclusions: Challenges in DM in LTC

- Glycemic targets in our older patients should be modified based upon burden of comorbidity, functional status, and life expectancy.
 - Target A1C should generally be 7.5-8%
 - Consider A1C of 7-7.5% in healthy older adults w/ few comorbidities and good functional status.
 - Consider A1C of 8-9% for older adults w/ multiple comorbidities, poor health or limited life expectancy
- Hypoglycemia can be minimized by choosing agents with lower hypoglycemic risk, simplifying regimens, and limiting use of insulin sliding scale.
 - Can also decrease risk in insulin deficient patients with use of an insulin pump or CGM
 - Treat lows using the rule of 15.
- Insulin resistance may remind us to search for precipitants (infection, etc), ensure patient is not overinsulinized, and aim to use agents that help with weight loss.
 - Even in our elderly, lifestyle must be stressed.

CALTCM 2017

Quality Through Best Practices



2017 CALTCM Annual Meeting

Quality Through Best Practices

April 28 & 29, 2017

CALTCM 2017

Quality Through Best Practices