HbA1c Poor Control:
Patient Education and Engagement

Presenters:

Andrew J. Ahmann M.D., Professor of Medicine, Division of Endocrinology, Diabetes and Clinical Nutrition School of Medicine and Harold Schnitzer Director of the Harold Schnitzer Diabetes Health Center

Sarah Wetherson, MA, Transformation Analyst, Oregon Health Authority

Hosted by:
Oregon Health Authority Transformation Center

Oregon Health Authority

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Financial relationship disclosures

Andrew Ahmann, MD: see table below.
Nancy Elder, MD, MSPH: no disclosures
Sarah Wetherson: no disclosures.

Name of commercial interest	Who has the relationship?	What is the relationship?		What was received?	Please provide a brief explanation of how this relationship does not cause a conflict of interest.
Novo Nordisk	myself	Consultant		Consulting Fees	The programs will be evidence based and use no brand names. Recommendations for therapy will emphasize classes of medications and strictly adhere to national guidelines (e.g. American Diabetes Association guidelines.
Lilly	myself	Consultant		Consulting Fees	The programs will be evidence based and use no brand names. Recommendations for therapy will emphasize classes of medications and strictly adhere to national guidelines (e.g. American Diabetes Association guidelines.
Dexcom	myself	Investigator	local PI for research studiies developing continuous glucose monitoring advances	Grant Support	CGM is not part of the discussion topics.
Medtronic	myself	Consultant	Expert advisory board	Consulting Fees	Relationship unrelated to subject matter of this program. Insulin pumps will not be addressed.

Getting CME credit

- After this webinar, we'll send a link to the post-test and evaluation
- Please complete the post-test (with a passing score) and evaluation within 3 weeks
- Certificates will come from OHSU within 8 weeks

Addressing Poor HbA1c Control: Clinic-based Solutions:

Patient Education and Engagement

PRESENTED BY: Andrew Ahmann, MD

Reviewing the importance of controlling diabetes.

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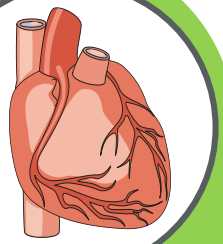
Diabetes Statistics

- 30.3 millions have diabetes in the US
  - 9.4% of the population
  - 12.2% of adults
- Rates higher for American Indians, Blacks and Hispanic
- 33.9% of US adults have prediabetes
- 2017 costs estimated at $327 billion in US
  - Costs are increasing rapidly (26% from 2012-2017)
- Costly complications of diabetes are decreasing but rates remain much higher than the general population.

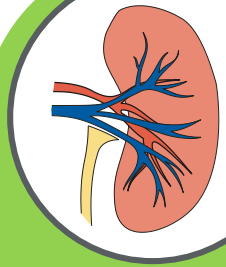
National Diabetes Statistics Report, 2017 (CDC)
American Diabetes Association, Diabetes Care 2018; 41:917-928

Clinical Impact of Diabetes

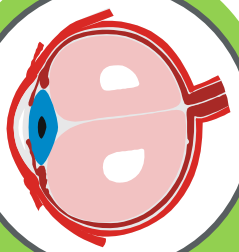
Diabetes



2- to 4-fold increase in cardio-vascular disease



Leading cause of new cases of kidney failure



Leading cause of new cases of blindness in working-aged adults

Leading cause of lower extremity amputations

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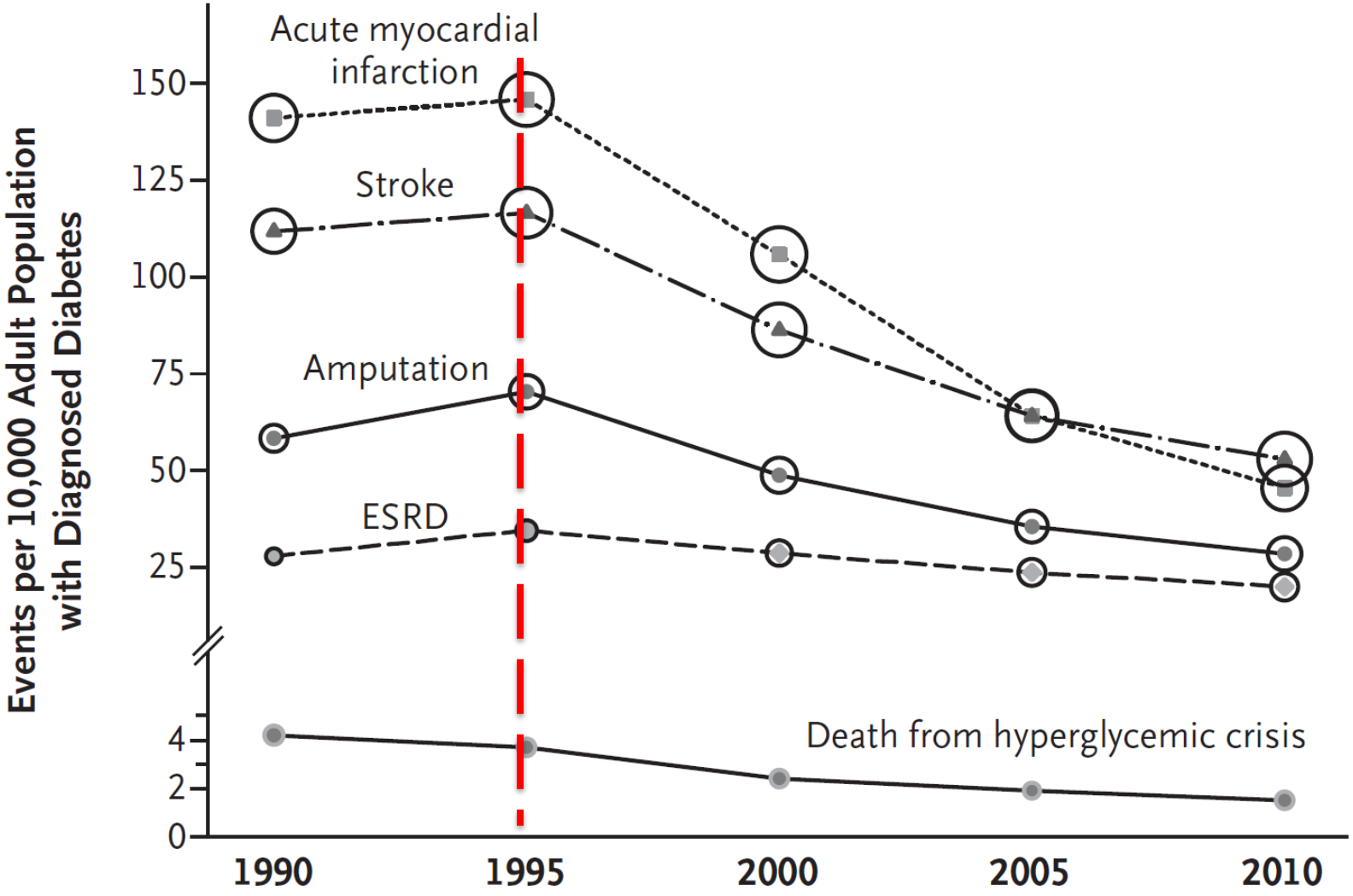
Changes in Diabetes Related Complications from 1990-2010



Gregg EW et al. N Engl J Med 2014; 370:514-523

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Changes in Diabetes Complication Rates

Complication	% Reduction	Relative Rate
MI with DM	**- 67.8**	1.8
MI without DM	-31.2	
Stroke with DM	**-52.7**	1.5
Stroke without DM	- 5.5	
LEA with DM	**- 57.4**	2.7
LEA without DM	- 12.9	
ESRD with DM	**- 28.3**	6.1
ESRD without DM	+ 65	

- Data from National Health Interview Survery, National Hospital Discharge Survey, US Renal Data System and US National Vital Statistics System
- 1990-2010

Gregg EW et al. N Engl J Med 2014; 370: 514-523

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ADA Standards of Care 1989

- First published standards of care
- Publication was 4 pages long
- No specific recommendations for:
  - Glucose control
  - BP control
  - Lipid management
  - Eye care (only referral to ophthalmology)
  - Foot exam
  - Kidney evaluation or management

Diabetes Care 1989; 12:365-368

ADA Standards of Care 2004

- Was up to 21 pages, evidence graded
- Had recommendations for:
  - Glucose control – A1C < 7.0%
  - BP control – target < 130/80
    - ACEI or ARBs 1st line; usually 2 or more agents
  - CVD Prevention
    - Use statin if over age 40
    - Target LDL < 100 or 30% reduction
    - Smoking cessation
  - Eye care – yearly dilated exam
  - Foot exam – monofilament or other yearly
  - Kidney evaluation or management
    - Microalbumin checking yearly – ACEI or ARB if +

Require comprehensive approach to maximize reduction of complications.

Diabetes Care 2004, Suppl 1

ADA Standards of Care 2020

- Now 212 pages in 16 sections
- Population health:
  - Team approach with collaborative effort including patient
  - Treatment decisions must be evidence based
  - **Employ Chronic Care Model**, use registries, decisions support tools
  - **Utilize lay health coaches and community health workers**
  - Always assess social context
  - Identify patients with pre-diabetes
    - Refer to a Diabetes Prevention Program

Diabetes Care 2020; 43(Suppl 1): S1-S212

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Chronic Care Model

The Chronic Care Model includes six core elements to optimize the care of patients with chronic disease:

1. Delivery system design (moving from a *reactive* to a *proactive* care delivery system where planned visits are coordinated through a team-based approach)
2. Self-management support
3. Decision support (basing care on evidence-based, effective care guidelines)
4. Clinical information systems (using registries that can provide patient-specific and population-based support to the care team)
5. Community resources and policies (identifying or developing resources to support healthy lifestyles)
6. Health systems (to create a quality-oriented culture)

Improving Care and Promoting Health in Populations:
Standards of Medical Care in Diabetes - 2019. *Diabetes Care* 2019;42(Suppl. 1):S7-S12

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ADA Standards of Care 2020

- Important to have diabetes self-management education and support
  - Patient centered
  - Should be reimbursed
  - Nutrition recommendations are individualized
  - Most adults should get 150 minutes of moderate intensity exercise per week
- Individualize A1C goals
  - Depends on age, co-morbidities, complications, risk of hypoglycemia.

Diabetes Care 2020; 43(Suppl 1): S1-S212

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Balancing Risks and Benefits for Personalized Goals

More Stringent Control

- No hypoglycaemia
- Less complexity/polypharmacy
- Lifestyle or metformin only
- Short disease duration
- Long life expectancy
- No CVD

Less Stringent Control

- History of severe hypoglycaemia
- High burden of therapy
- Longer disease duration
- Limited life expectancy
- Extensive co-morbidity
- CVD

- A1C Goal for most nonpregnant adults is < 7.0%
- Goal is set with patient and should be higher for some (e.g. 7-8%)

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ADA Standards of Care 2020

- Patient glucose monitoring depending on agents and intensity of insulin therapy
- Monitor/ treat high blood pressure
- CVD Prevention beyond BP
  - Statins for most over 40 years of age
  - T2DM w ASCVD, SGLT2i or GLP-1 RA
  - Identify, treat microvascular complications
  - e.g. microalbumin testing and eye exams
- For older adults:
  - Screen for cognitive deficits
  - High priority to avoid hypoglycemia and falls

Diabetes Care 2020; 43(Suppl 1): S1-S212

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What is Accomplished in a Visit

- Review interim history
  - Success in accomplishing previously stated goals
  - Any changes in diet or activity or stressors
  - ROS focusing on diabetes complications / comobidities
- Review of diabetes specific health maintenance
- Pertinent physical exam (e.g. feet)
- Review of data:
  - A1C, BGs, Lipids, microalbumin
- Allow patient to ask questions
- Discuss potential changes in therapy or goals
  - **Involve patient in the decision.**
- Identify patient specific barriers in self-management
  - Identify need for diabetes education and support

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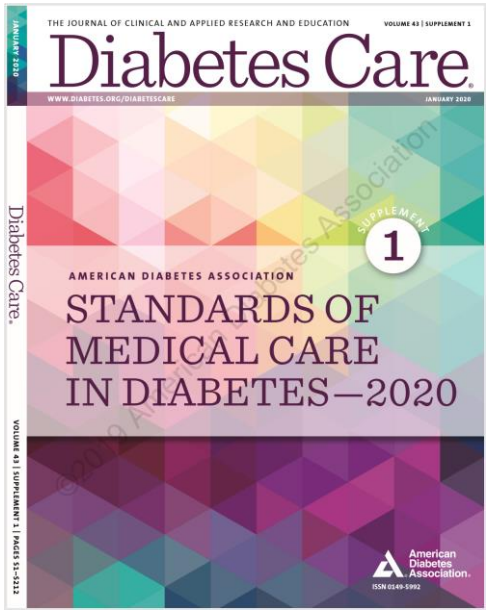
Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

Melanie J. Davies,[1,2] David A. D'Alessio,[3] Judith Fradkin,[4] Walter N. Kernan,[5] Chantal Mathieu,[6] Geltrude Mingrone,[7,8] Peter Rossing,[9,10] Apostolos Tsapas,[11] Deborah J. Wexler,[12,13] and John B. Buse[14]

Diabetes Care 2018;41:2669–2701 | https://doi.org/10.2337/dci18-0033

Incorporated into the ADA Standards of Care in the January 2020 supplement of *Diabetes Care and updated*



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Components of Hyperglycemic Management

Lifestyle

- Medical Nutrition Therapy
- Physical activity

Medications

Metabolic Surgery

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Foundational therapy is metformin and comprehensive lifestyle management (including weight management and physical activity)

For Details on Each Medication Please See . . . .

Table 9.1—Drug-specific and patient factors to consider when selecting antihyperglycemic treatment in adults with type 2 diabetes

	Efficacy	Hypoglycemia	Weight change	CV effects		Cost	Oral/SQ	Renal effects		Additional considerations
				ASCVD	CHF			Progression of DKD	Dosing/use considerations*	
Metformin	High	No	Neutral (potential for modest loss)	Potential benefit	Neutral	Low	Oral	Neutral	▪ Contraindicated with eGFR <30	▪ Gastrointestinal side effects common (diarrhea, nausea) ▪ Potential for B12 deficiency
SGLT-2 inhibitors	Intermediate	No	Loss	Benefit: empagliflozin†, canagliflozin	Benefit: empagliflozin†, canagliflozin	High	Oral	Benefit: canagliflozin, empagliflozin	▪ Renal dose adjustment required (canagliflozin, dapagliflozin, empagliflozin, ertugliflozin)	▪ **FDA Black Box:** Risk of amputation (**canagliflozin**) ▪ Risk of bone fractures (canagliflozin) ▪ DKA risk (all agents, rare in T2DM) ▪ Genitourinary infections ▪ Risk of volume depletion, hypotension ▪ ↑LDL cholesterol ▪ Risk of Fournier's gangrene
GLP-1 RAs	High	No	Loss	Neutral: lixisenatide Benefit: liraglutide† > semaglutide > exenatide extended release	Neutral	High	SQ	Benefit: liraglutide	▪ Renal dose adjustment required (exenatide, lixisenatide) ▪ Caution when initiating or increasing dose due to potential risk of acute kidney injury	▪ **FDA Black Box:** Risk of thyroid C-cell tumors (**liraglutide, albiglutide, dulaglutide, exenatide extended release**) ▪ Gastrointestinal side effects common (nausea, vomiting, diarrhea) ▪ Injection site reactions ▪ ?Acute pancreatitis risk
DPP-4 inhibitors	Intermediate	No	Neutral	Neutral	Potential risk: saxagliptin, alogliptin	High	Oral	Neutral	▪ Renal dose adjustment required (sitagliptin, saxagliptin, alogliptin); can be used in renal impairment ▪ No dose adjustment required for linagliptin	▪ Potential risk of acute pancreatitis ▪ Joint pain
Thiazolidinediones	High	No	Gain	Potential benefit: pioglitazone	Increased risk	Low	Oral	Neutral	▪ No dose adjustment required ▪ Generally not recommended in renal impairment due to potential for fluid retention	▪ **FDA Black Box:** Congestive heart failure (**pioglitazone, rosiglitazone**) ▪ Fluid retention (edema; heart failure) ▪ Benefit in NASH ▪ Risk of bone fractures ▪ Bladder cancer (pioglitazone) ▪ ↑LDL cholesterol (rosiglitazone)
Sulfonylureas (2nd generation)	High	Yes	Gain	Neutral	Neutral	Low	Oral	Neutral	▪ Glyburide: not recommended ▪ Glipizide and glimepiride: initiate conservatively to avoid hypoglycemia	▪ FDA Special Warning on increased risk of cardiovascular mortality based on studies of an older sulfonylurea (tolbutamide)
Insulin — Human Insulin	Highest	Yes	Gain	Neutral	Neutral	Low	SQ	Neutral	▪ Lower insulin doses required with a decrease in eGFR; titrate per clinical response	▪ Injection site reactions ▪ Higher risk of hypoglycemia with human insulin (NPH or premixed formulations) vs. analogs
Insulin — Analogs						High	SQ			

*For agent-specific dosing recommendations, please refer to the manufacturers' prescribing information. †FDA approved for CVD benefit. CHF, congestive heart failure; CV, cardiovascular; DPP-4, dipeptidyl peptidase 4; DKA, diabetic ketoacidosis; DKD, diabetic kidney disease; GLP-1 RAs, glucagon-like peptide 1 receptor agonists; NASH, nonalcoholic steatohepatitis; SGLT2, sodium–glucose cotransporter 2; SQ, subcutaneous; T2DM, type 2 diabetes.

ADA Standards of Care in Diabetes Care 2020; 43(suppl 1): S101

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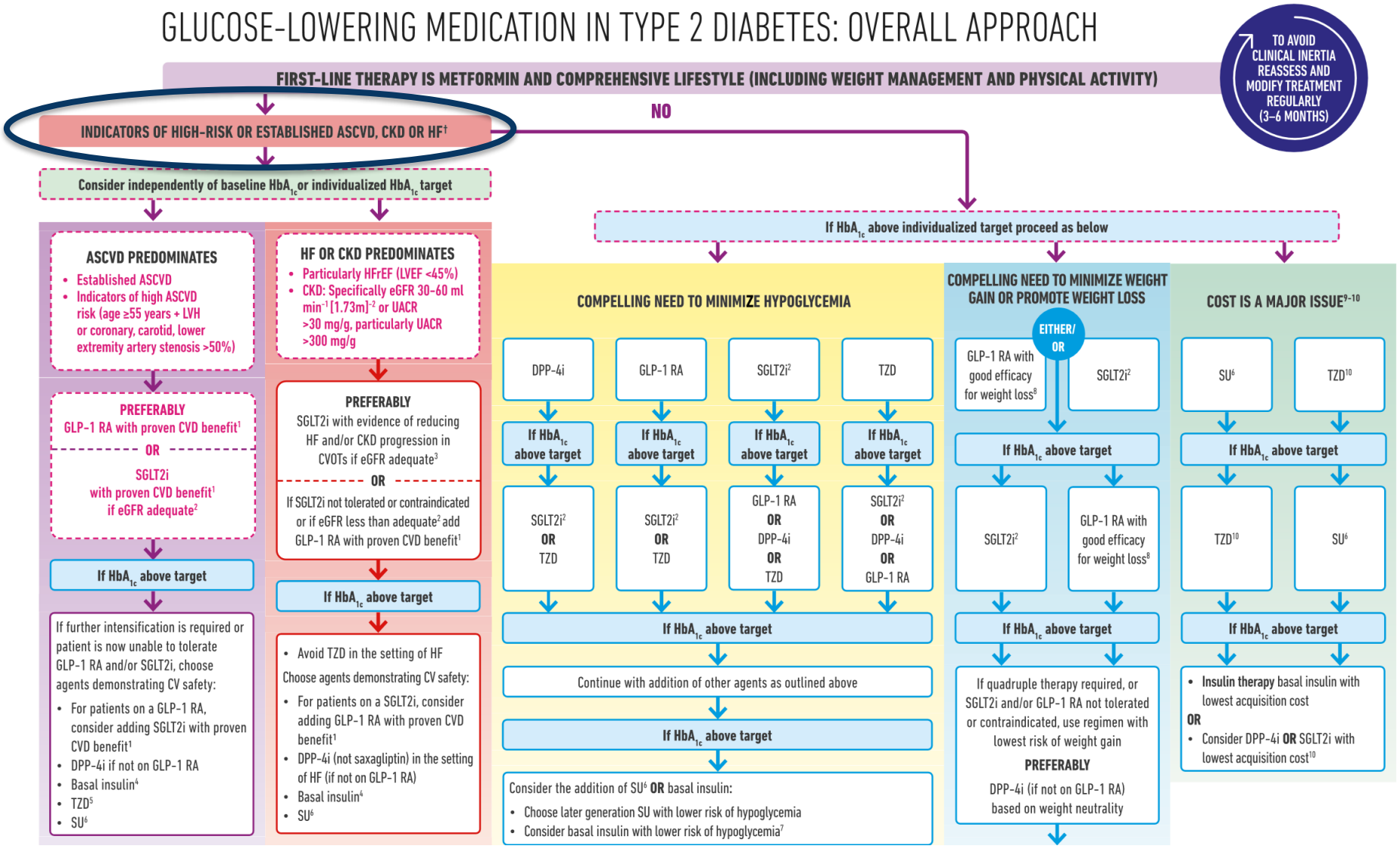
GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH



Buse, JB et al. Diabetes Care 2019; 43:487-93

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But diabetes management is much more than prescribing the best medications!

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Barriers To Successful Diabetes Management

- Provider inertia - - Delay in progression of therapy to reach target
- Behavioral barriers
- Non-adherence
- Hypoglycemia
- Weight gain
- **Lack of knowledge**
- Physical disability
- Cultural factors and language barriers
- Personal health beliefs
- Costs/ financial resources

Adapted from Funnell MM. *Clinical Diabetes*. 2007;25(1):36-38. Derr RL, et al. *Diabetes Spectrum*. 2007; 20(3):177-185. Karter AJ, et al. *Diabetes Care.* 2010;33(4):733-735.

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Medication Adherence in Diabetes

- Varies with population but 35-45% of patients are not adherent (< 80% of doses taken) over time
- Poor adherence is documented to correlate with higher morbidity, mortality and hospitalization
- Adherence varies by ethnicity
  - e.g. lower in Latinos, particularly if limited English proficiency
- Is often overlooked by clinicians
  - e.g. insulin doses are increased without consideration of missed dose causing the higher A1C

Khunti K et al Diabetes Care 2017; 40:1588. Huber CA et al Medicine 2016; 95:26. Capoccia K et al Diab Educator 2016; 42:34

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Factors Influencing Adherence

- Knowledge
- Patient involvement in goal setting and treatment decisions
- Socioeconomic factors
- Cultural factors
- Frequency of visits/ communications (cadence)
- Number of medications
- Frequency of dosing - - < vs > twice daily
- Hypoglycemia / side effects
- Weight gain
- Disabilities
- Satisfaction with their care

Khunti K et al Diabetes Care 2017; 40:1588. Huber CA et al Medicine 2016; 95:26.
Capoccia K et al Diab Educator 2016; 42:34

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Diabetes Medications Can Be Costly

Table 9.2—Median monthly cost of maximum approved daily dose of noninsulin glucose-lowering agents in the U.S.

Class	Compound(s)	Dosage strength/product (if applicable)	Median AWP (min, max)†	Median NADAC (min, max)†	Maximum approved daily dose*
Biguanides	• Metformin	500 mg (IR)	$84 ($4, $93)	$2	2,000 mg
		850 mg (IR)	$108 ($6, $109)	$3	2,550 mg
		1,000 mg (IR)	$87 ($4, $88)	$2	2,000 mg
		500 mg (ER)	$89 ($82, $6,671)	$4 ($4, $1,267)	2,000 mg
		750 mg (ER)	$72 ($65, $92)	$4	1,500 mg
		1,000 mg (ER)	$1,028 ($1,028, $7,214)	$311 ($311, $1,321)	2,000 mg
Sulfonylureas (2nd generation)	• Glimepiride	4 mg	$71 ($71, $198)	$4	8 mg
	• Glipizide	10 mg (IR)	$75 ($67, $97)	$5	40 mg (IR)
		10 mg (XL)	$48	$15	20 mg (XL)
	• Glyburide	6 mg (micronized)	$50 ($48, $71)	$10	12 mg (micronized)
		5 mg	$93 ($63, $103)	$13	20 mg
Thiazolidinediones	• Pioglitazone	45 mg	$348 ($283, $349)	$4	45 mg
	• Rosiglitazone	4 mg	$407	$329	8 mg
α-Glucosidase inhibitors	• Acarbose	100 mg	$106 ($104, $106)	$23	300 mg
	• Miglitol	100 mg	$241	$311	300 mg
Meglitinides (glinides)	• Nateglinide	120 mg	$155	$46	360 mg
	• Repaglinide	2 mg	$878 ($162, $898)	$48	16 mg
DPP-4 inhibitors	• Alogliptin	25 mg	$234	$170	25 mg
	• Saxagliptin	5 mg	$490 ($462, $490)	$392	5 mg
	• Linagliptin	5 mg	$494	$395	5 mg
	• Sitagliptin	100 mg	$516	$413	100 mg
SGLT2 inhibitors	• Ertugliflozin	15 mg	$322	$257	15 mg
	• Dapagliflozin	10 mg	$557	$446	10 mg
	• Canagliflozin	300 mg	$558	$446	300 mg
	• Empagliflozin	25 mg	$558	$448	25 mg
GLP-1 receptor agonists	• Exenatide (extended release)	2 mg powder for suspension or pen	$792	$634	2 mg**
	• Exenatide	10 μg pen	$850	$680	20 μg
	• Dulaglutide	1.5/0.5 mL pen	$876	$702	1.5 mg**
	• Semaglutide	1 mg pen	$875	$704	1 mg**
	• Liraglutide	18 mg/3 mL pen	$1,044	$835	1.8 mg
Bile acid sequestrants	• Colesevelam	625 mg tabs	$712 ($674, $712)	$354	3.75 g
		3.75 g suspension	$674	$598	3.75 g
Dopamine-2 agonists	• Bromocriptine	0.8 mg	$855	$685	4.8 mg
Amylin mimetics	• Pramlintide	120 μg pen	$2,547	$2,036	120 μg/injection†††

AWP, average wholesale price; DPP-4, dipeptidyl peptidase 4; ER and XL, extended release; GLP-1, glucagon-like peptide 1; IR, immediate release; NADAC, National Average Drug Acquisition Cost; SGLT2, sodium–glucose cotransporter 2. †Calculated for 30-day supply (AWP [44] or NADAC [45] unit price × number of doses required to provide maximum approved daily dose × 30 days); median AWP or NADAC listed alone when only one product and/or price. *Utilized to calculate median AWP and NADAC (min, max); generic prices used, if available commercially. **Administered

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CAROLINA Study
- Shows SU has CV Safety-

- Part of the CVOT on linagliptin using an active comparator
  - 5 mg linagliptin vs up to 4 mg glimepiride
- 6033 subjects with T2DM over mean 6.3 years
- Primary Outcome =

  MACE with CV Death, nonfatal MI or nonfatal stroke
- Results:
  - **No difference in primary outcome with HR 0.98** (95% CI 0.84-1.14)
  - No difference in CV morality (HR = 1.0)
  - No difference in A1C (glimepiride lower early but higher later)
  - 1.5 Kg lower weight with linagliptin
  - Much lower hypoglycemia with linagliptin

Presented at 79th ADA Scientific Sessions June 10, 2019 San Francisco

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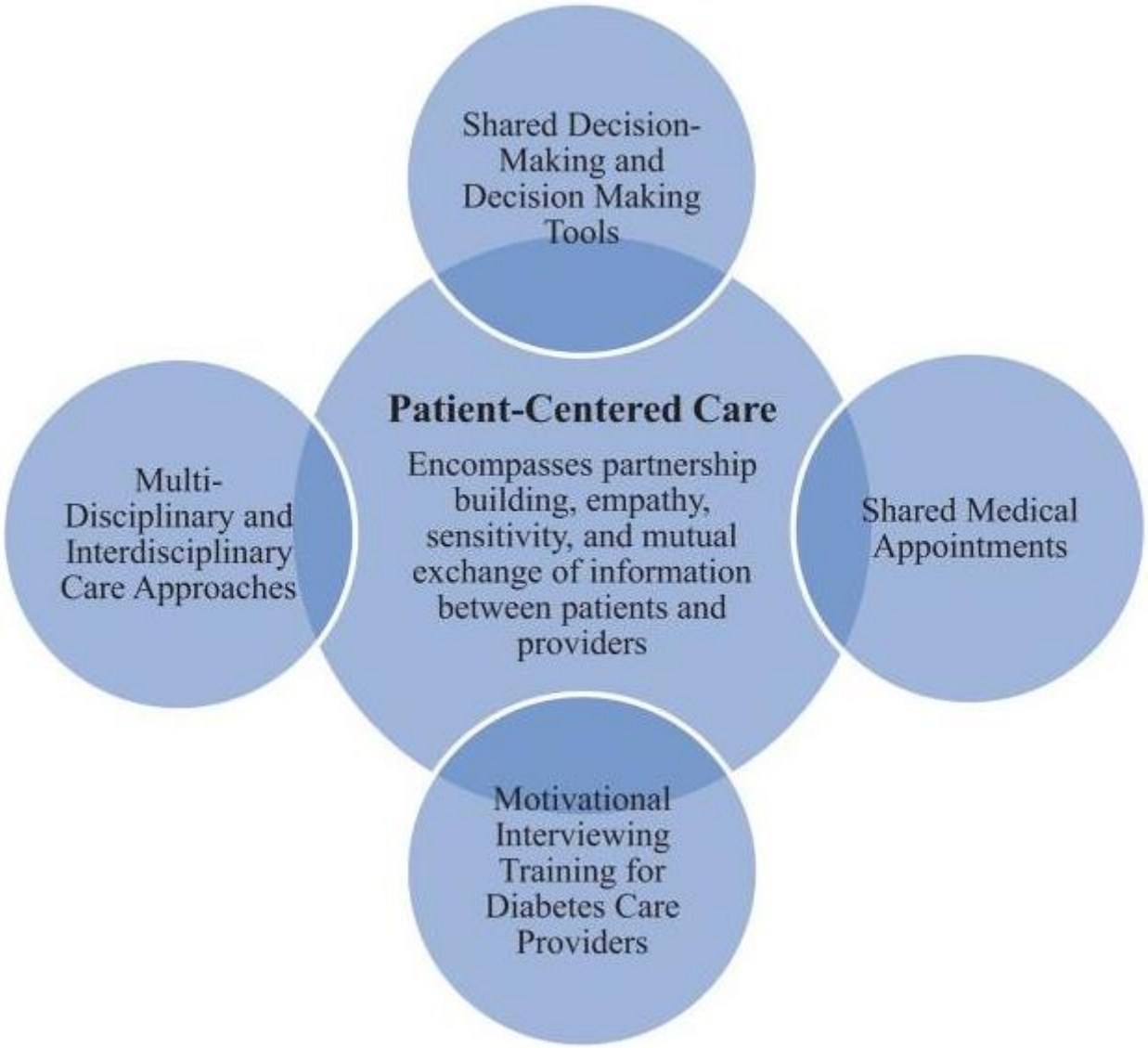

Powell PW et al Curr Diabetes rev 2015; 11:222-230

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Successful Diabetes Care is a Team Effort

- Diabetes educator (multiple training backgrounds)
- Pharmacist
- RD
- Care Coordinator
- Physician or APP
- Podiatrist
- Psychologists or social workers
- Ophthalmologist
- Specialists to manage complications
- Community Health Workers
- **The Patient!**

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Patient Engagement Is Crucial

- Improves health outcomes
- Improves quality of life
- Improves patient safety
- Helps control healthcare costs

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Patient Engagement Related Concepts

- Patient activation
- Patient involvement
- Patient participation
- Patient adherence/compliance
- Patient empowerment

Barello S et al. Frontiers in Psychology 2016; 6:1 (article 2013)

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Dimensions of Patient Engagement

- **Behavioral**
  - What the patient does
- **Cognitive**
  - What the patient thinks and knows
- **Emotional**
  - What the patient feels

Barello S et al. Frontiers in Psychology 2016; 6:1 (article 2013)

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Tools for Patient Engagement

- Shared decision making (SMD)
- Motivational interviewing
- eHealth options
  - Have been shown to decrease depressive symptoms, increase adherence, improves satisfaction, improved medical care team communications, reduce A1C
- Use of community health workers
- Diabetes education in various forms

Barello S et al. Frontiers in Psychology 2016; 6:1 (article 2013)

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Use of Empowering Language.

Five key consensus recommendations for language use:

1. Use language that is neutral, nonjudgmental, and based on factus, actions, or physiology/biology;
2. Use language that is free from stigma;
3. Use language that is strength based, respectful, and inclusive and that imparts hope;
4. Use language that fosters collaboration between patients and providers;
5. Use language that is person centered (e.g., “person with diabetes” is preferred over “diabetic”).

Comprehensive Medical Evaluation and Assessment of Comorbidities:
Standards of Medical Care in Diabetes - 2019. *Diabetes Care* 2019;42(Suppl. 1):S34-S45

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Figure 1

DECISION CYCLE FOR PATIENT-CENTRED GLYCAEMIC MANAGEMENT IN TYPE 2 DIABETES

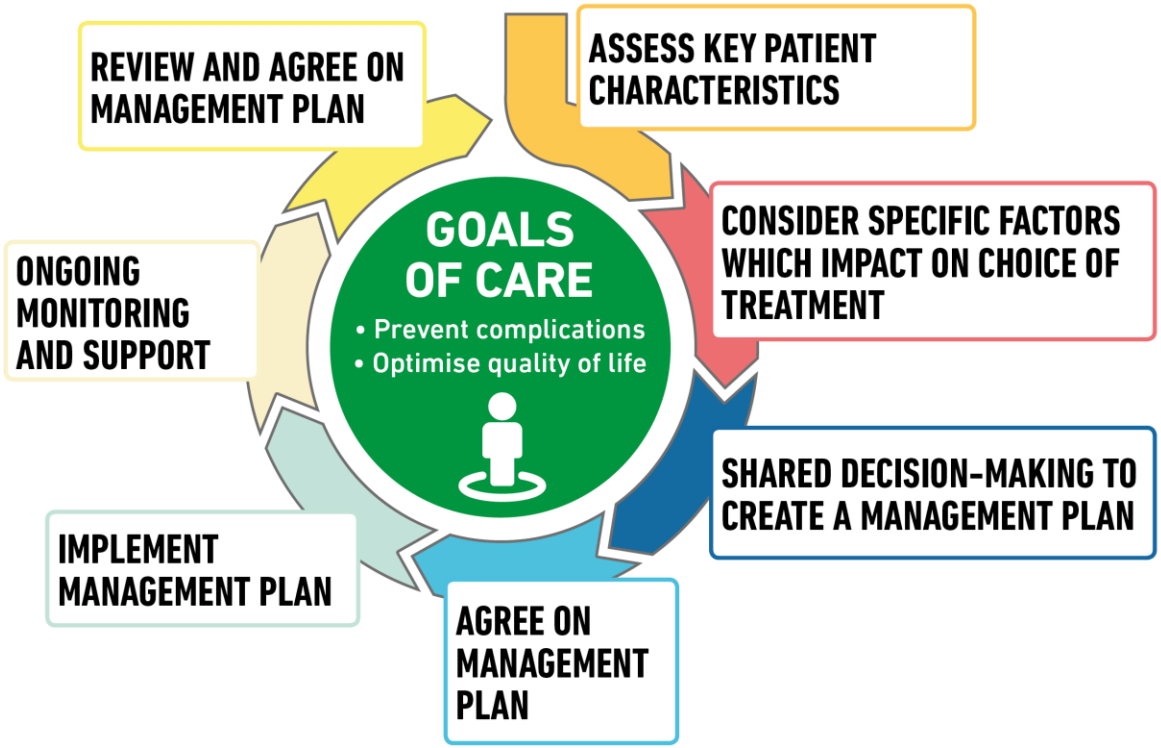

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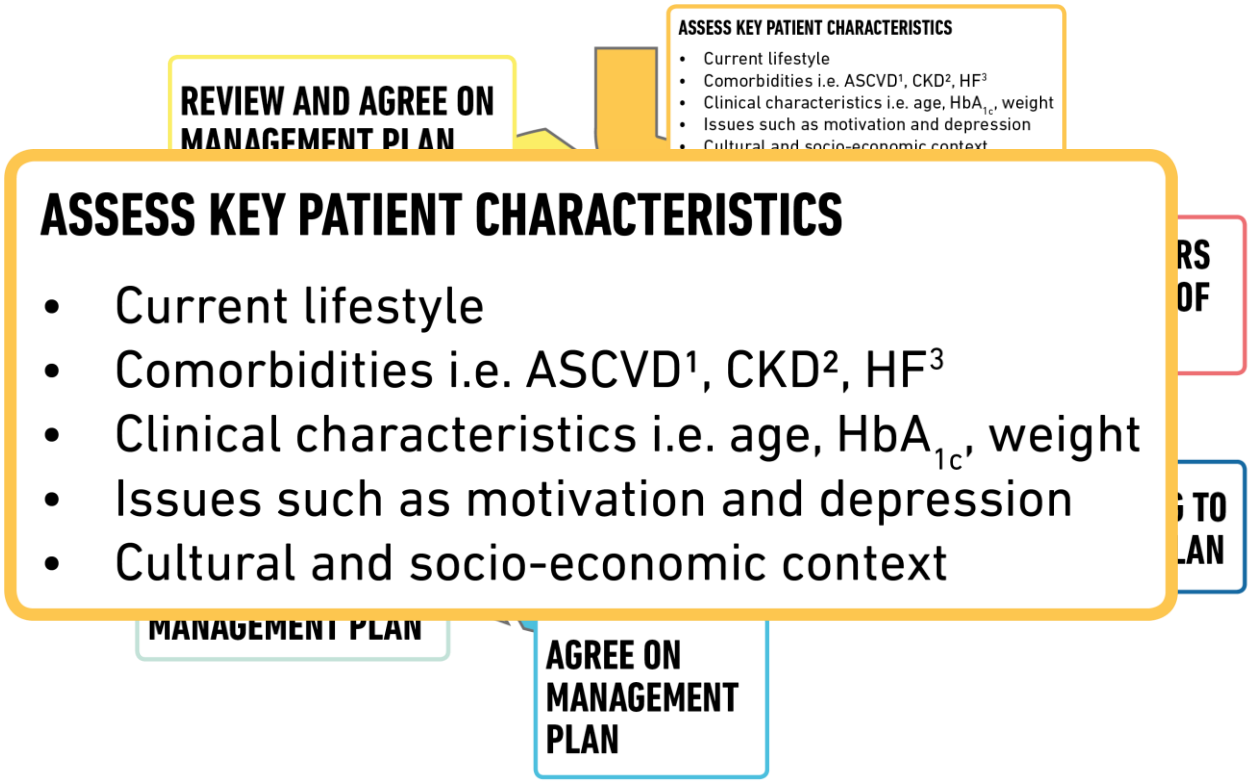
Figure 1

DECISION CYCLE FOR PATIENT-CENTRED GLYCAEMIC MANAGEMENT IN TYPE 2 DIABETES



Diabetes Self-Management Education and Support (DSMES)

- **Good evidence that DSMES results in**:
  - Improved diabetes knowledge
  - Improved self-care behaviors
  - Lower A1C
  - Improved quality of life
  - Reduced health care costs
  - Increased use of primary care and preventive services
  - Less use of inpatient services

ADA Standard of Medical Care – 2020. Diabetes Care 2020; 43(suppl 1): S48-S65

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Diabetes Self-Management Education and Support: Delivery.

Four critical time points for DSMES delivery:

1. At diagnosis;
2. Annually for assessment of education, nutrition, and emotional needs;
3. When new complicating factors (health conditions, physical limitations, emotional factors, or basic living needs) arise that influence self-management; and
4. When transitions in care occur such as new meds or progressive renal insufficiency

DSMES is among the recommended standards of care that is most overlooked. Only 5-7% receive formal education.

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Diabetes Self-Management Education and Support (DSMES)

Important Features:

- Should be developed and delivered by those with specialized clinical knowledge on diabetes
  - Preference is Certified Diabetes Educators (CDEs)
  - Community health workers and peer leaders can provide important support
- Should be patient centered
- Communication with the full healthcare team

ADA Standard of Medical Care – 2020. Diabetes Care 2020; 43(suppl 1): S48-S65

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Diabetes Self-Management Education and Support: Key Components

- Nutrition therapy – more diversity in options
- Physical activity – what can be maintained
- Medications
  - Proper use
  - Side effects
  - Hypoglycemia recognition and treatment
- Monitoring
- Identifying and addressing management barriers
  - Psychological issues such as diabetes distress
  - Cultural issues
  - Financial

ADA Standard of Medical Care – 2020. Diabetes Care 2020; 43(suppl 1): S48-S65

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Nutrition Therapy for Adults With Diabetes or Prediabetes: A Consensus Report

Diabetes Care 2019;42:731–754 | https://doi.org/10.2337/dci19-0014

Alison B. Evert,[1] Michelle Dennison,[2] Christopher D. Gardner,[3] W. Timothy Garvey,[4,5] Ka Hei Karen Lau,[6] Janice MacLeod,[7] Joanna Mitri,[8] Raquel F. Pereira,[9] Kelly Rawlings,[10] Shamera Robinson,[11] Laura Saslow,[12] Sacha Uelmen,[11] Patricia B. Urbanski,[13] and William S. Yancy Jr.[14,15]

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Overcoming the Barriers to Insulin Therapy

- Avoid using insulin as a “threat,” but a solution and discuss it as an option early
- Use insulin pens and regimens that offer maximum flexibility
- **Give a “limited” trial of insulin**
- Tell patient injection is less painful than finger stick and give an injection in the office
- **Teach patient to recognize and treat hypoglycemia, and use basal analog insulins to minimize hypoglycemia risk**
- Meet with dietitian before initiation of insulin

Kruger D, et al. *Diabetes Educ*. 2010;36(suppl 3):44S-72S. Funnell MM. *Clinical Diabetes*. 2007;25(1):36-38. Derr RL, et al. *Diabetes Spectrum*. 2007; 20(3):177-185.

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Summary

- Diabetes management is complex and requires a collaborative effort
  - Multidisciplinary team
  - The patient at the center
- Team members must be aware of standards of care
- Diabetes education is paramount
- Goals and treatments need to be individualized.
- Many meds are available
  - Selections of agents is affected by CV status
- Adherence to lifestyle modification and medications is a major factor in success.

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Thank You!

Thank you!

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Oregon Health Authority Transformation Center.

- For more information about this presentation, contact Transformation.Center@state.or.us
- Find more resources for diabetes care here: https://www.oregon.gov/oha/HPA/dsi-tc/Pages/Diabetes.aspx
- Sign up for the Transformation Center's technical assistance newsletter: https://www.surveymonkey.com/r/OHATransformationCenterTA