A Systems Approach to Improving Diabetes Care

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

Kate Lonborg, Clinical Quality Metrics Registry Program Manager, Oregon Health Authority

Sarah Wetherson, MA, Transformation Analyst, Oregon Health Authority

Hosted by:
Oregon Health Authority Transformation Center



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HEALTH POLICY AND ANALYTICS Transformation Center



Kate Lonborg, Clinical Quality Metrics Registry Program Manager, Oregon Health Authority



Sarah Wetherson, MA, Transformation Analyst, Oregon Health Authority



Metric Background: Basic Specs

- Overview: Percentage of patients 18-75 years of age with diabetes who had hemoglobin A1c > 9.0% during the measurement period (<u>a lower score is</u> <u>better</u>).
- Data Source: EHR; electronic Clinical Quality Measure (eCQM)
- Equation:

Patients whose most recent HbA1c level (performed during the measurement period) is >9.0%.

Patients 18-75 years of age with diabetes with a visit during the measurement period (diabetes is identified using the Diabetes Grouping Value Set - 2.16.840.1.113883.3.464.1003.103.12.1001).



Metric Background: Basic Specs

Diabetes Care: HbA1c Poor Control

Percentage of patients 18-75 years of age with diabetes who had hemoglobin A1c > 9.0% during the measurement period. A lower score is better.

Data source:

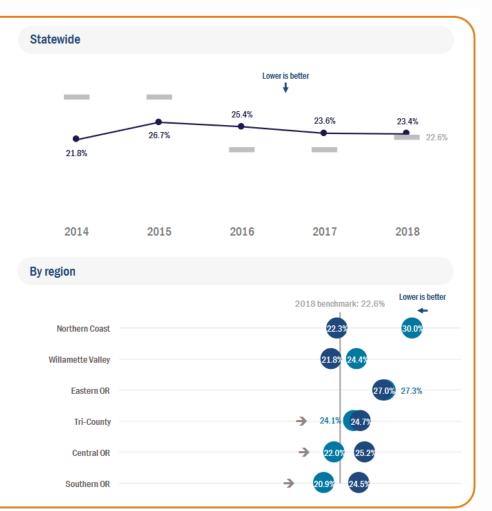
Electronic Health Records

2018 benchmark source:

2016 CCO 90th percentile

2018 data (N=54,664)

- Statewide change since 2017: -0.8%
- Number of CCOs that improved: 6
- Number of CCOs achieving target: 7



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HEALTH POLICY AND ANALYTICS
Transformation Center



Metric Background: Poor Control Defined

 Continuous Enrollment Criteria: None. The "eligible as of the last date of the reporting period" rule may be used to identify beneficiaries to be included in the measure.

NB:

- Only patients with a diagnosis of Type 1 or Type 2 diabetes are included in the denominator; patients with a diagnosis of secondary diabetes due to another condition are not be included.
- Patient is numerator compliant if:
 - The most recent HbA1c level >9%;
 - The most recent HbA1c result is missing, or,
 - If there are no HbA1c tests performed and results documented during the measurement period.
- Exclusions: Patients in hospice. Beginning in 2020 (<u>CMS122v8</u>), the measure steward, NCQA, added new exclusions for patients aged 66+ who (1) are living long term in an institution for 90+ days or (2) have advanced illness and frailty.



Metric Background: Evidence Base

- Diabetes is the 7th leading cause of death in the U.S.
- People with diabetes are at increased risk of serious health complications, including:
 - Vision loss
 - Heart disease
 - Stroke

- Kidney failure
- Amputation of toes, feet or legs
- Premature death
- In 2012, diabetes cost the U.S. ~\$245B
 - \$176 billion direct medical costs
- \$69 billion reduced productivity
- Reducing HbA1c level by 1 percentage point helps reduce risk of microvascular complications by as much as 40 percent.

https://ecqi.healthit.gov/sites/default/files/ecqm/measures/CMS122v7.html





Conflict of Interest

- I have the following Conflicts of Interest to report
 - ♦ Grants/Research
 - Lilly, Dexcom
 - ♦ Consultant
 - Lilly, Novo Nordisk, Medtronic
- Any non-approved medication use will be identified.



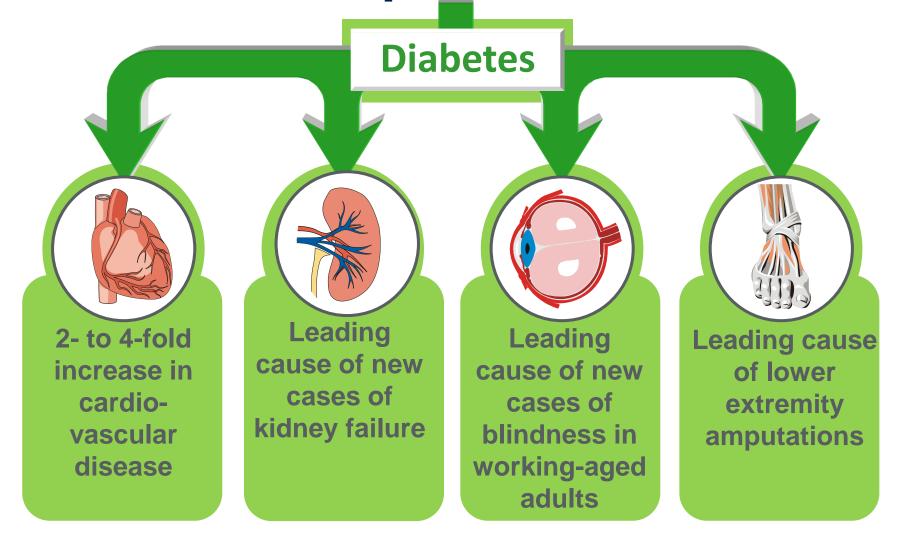
Reviewing the importance of controlling diabetes.



Diabetes Statistics

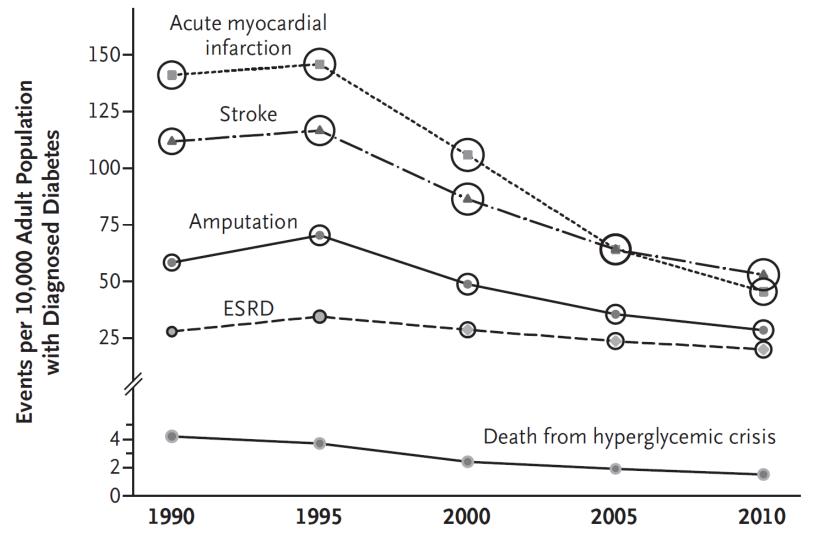
- 30.3 millions have diabetes in the US
 - 9.4% of the population
 - 12.2% of adults
- Rates higher for American Indians, Blacks and Hispanic
- 33.9% of US adults have prediabetes
- 2017 costs estimated at \$327 billion in US
 - Costs are increasing rapidly (26% from 2012-2017)
- Costly complications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

Clinical Impact of Diabetes





Changes in Diabetes Related Complications from 1990-2010





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



What We Know About Benefit of Glucose Control In Type 2 Diabetes

- Microvascular complications (including neuropathy)
 - Benefit with early intervention
 - UKPDS
 - Benefit from later improvements in glucose control
 - ACCORD
 - ADVANCE
 - VADT

Macrovascular complications

- Long-term benefit with early intervention
 - UKPDS, confirmed on extension
- No significant benefit shown in those intensified later
 - ACCORD, ADVANCE



Diabetes Management is More Than Glucose Control

- Has become very clear that comprehensive care is paramount
 - Glucose control
 - BP control
 - CV risk management including statins
 - Education
 - Complication surveillance
 - Microalbumin testing and lipid testing
- Employs the Chronic Disease Model
- Must consider the social context



- 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



- 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 +



- 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, community health workers and other community resources
 - Always assess social context
 - Identify patients with pre-diabetes
 - Refer to a Diabetes Prevention Program



- 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.



- Check A1C at least twice yearly
 - Target depends on age, co-morbidities, complications, risk of hypoglycemia.
- Ask about hypoglycemia any time the patient is on an agent that can cause hypoglycemia
- Patient glucose monitoring depending on agents and intensity of insulin therapy



- Monitor blood pressure
 - Treat with medication if ≥140/90
 - Goal is ≤ 130/80 for those with high CV risk
 - 10-year CV risk $\geq 15\%$
- CVD Prevention beyond BP
 - Moderate intensity statin in patients without CV disease age 40-75
 - If patient has CV disease or very high risk ► high dose
 - If 10 year risk ≥ 20% and LDL ≥ 70 mg/dl or LDL decrease >50%
 - Add ezetimibe or PCSK9 inhibitors
 - T2DM w ASCVD, SGLT2i or GLP-1 RA if A1C elevated
- ASA for secondary prevention



- Screening for microvascular complications
 - Microalbumin:creatinine ratio yearly (repeat if +)
 - Eye exam yearly
 - Comprehensive foot exam yearly
- Treat microvascular complications
 - Nephropathy - ACEI/ARB, BP ↓, A1C ↓, SGLT2 inh
 - Eyes - Glucose control, laser Tx, VEGF
 - Neuropathy - A1C ↓, special footwear for highest risk
- For older adults:
 - Screen for cognitive deficits
 - High priority to avoid hypoglycemia



What is Accomplished in a Visit

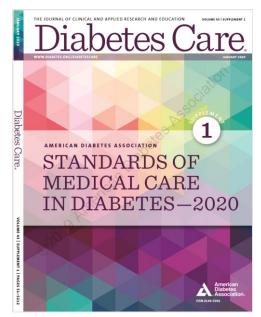
- Review interim history
 - Success in accomplishing previously stated goals
 - Any changes in diet or activity or stressors
 - ROS focusing on diabetes complications / comobidities
- Review of diabetes specific health maintenance
- Pertinent physical exam (e.g. feet)
- Review of data:
 - A1C, BGs, Lipids,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



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. Buse¹⁴

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*





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



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

Shared Decision-Making and Decision Making Tools

Multi-Disciplinary and Interdisciplinary Care Approaches

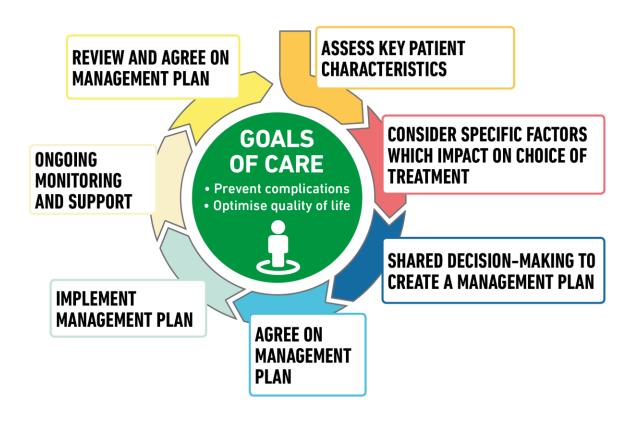
Patient-Centered Care

Encompasses partnership building, empathy, sensitivity, and mutual exchange of information between patients and providers

Shared Medical Appointments

Motivational Interviewing Training for Diabetes Care Providers







REVIEW AND AGREE ON MANAGEMENT PLAN

ASSESS KEY PATIENT CHARACTERISTICS

- Current lifestyle
- Comorbidities i.e. ASCVD¹, CKD², HF³
- Clinical characteristics i.e. age, HbA_{1c}, weight
- Issues such as motivation and depression
- Cultural and socio-economic context

ASSESS KEY PATIENT CHARACTERISTICS

- Current lifestyle
- Comorbidities i.e. ASCVD¹, CKD², HF³
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- Cultural and socio-economic context

MANAGEMENI PLAN

AGREE ON MANAGEMENT PLAN RS OF

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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%)

Don't overlook that reduction of A1C from 10% to < 9.0% results in greater risk reduction than reducing from 8% to < 7 %.



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



Components of Hyperglycemic Management

Lifestyle

- Medical Nutrition Therapy
- Physical activity

Medications

Metabolic Surgery



Diabetes Self-Management Education and Support: Delivery.

Four critical time points for DSMES delivery:

- 1. At diagnosis;
- 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



Facilitating Behavior Change

- At least as important as medications
- Includes:
 - Diabetes Self-Management Education & Support
 - Psychologist as a major facilitator
 - Recognize diabetes distress
 - Help patient and team develop strategies to overcome individual barriers
 - Identify cognitive impairment and depression
 - Addressing socioeconomic barriers
- Remember that the patient is at the center of care
 - Patient manages her/his diabetes alone 99% of the time



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
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Shamera Robinson,¹¹ Laura Saslow,¹²
Sacha Uelmen,¹¹ Patricia B. Urbanski,¹³ and William S. Yancy Jr.^{14,15}

General principles are employed but diets must be individualized according to cultural preferences, economic considerations and patient preferences.



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	CV effects		Cost	Oral/SQ	Renal effects		
			A CONTRACTOR OF THE PARTY OF TH	change	ASCVD	CHF		Olatio	Progression of DKD	Dosing/use considerations*	Additional considerations
Wetformie	,	High	No	Neutral (potential for modest loss)	Potential benefit	Neutral	Low	Oral	Neutral	Contraindicated with eGFR < 30	Gastrointestinal side effects commo (diarrhea, nausea) Potential for B12 deficiency
SGLT-2 leh	ilbètors	Intermediate	No	Loss	Benefit: empagliflozin1, canagliflozin	Benefit: empagliflozin†, canagliflozin	High	Oral	Benefit cansgliflozin, empagliflozin	Renal dose adjustment required (canagifilozin, depagliflozin, empagliflozin, ertugliflozin)	FDA Black Box Risk of amputation (canagliflozin) Risk of bone fractures (canagliflozin) Dikarisk (all agents, rare in 720M) Genitourinary infections Risk of volume depletion, hypoteration ALC, cholesterol Risk of of Fournier's gangreene
GLP-1 RAS		Migh	No	Loss	Neutral: lixisenatide	Neutral	High	SQ	Benefit liragiutide	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 (Bragilutide, albighutide, dulagilutide, exenatide extended release) Gastrointestinal side effects common (hauses, vomiting, diatrihea) Injection site reactions 7-Acute pancreatitis risk
					Benefit: liraglutidet > sema- glutide > exenatide extended release						
DPP-4 inhi	ibitors	Intermediate	No	Neutral	Neutral	Potential risic saxagliptin, alogliptin	High	Oral	Neutral	Renal doce adjustment required (sitagliptin, savagiptin, adjulptin); can be used in renal impairment No doce adjustment required for linagliptin	Potential risk of acute pancrestitis Joint pain
Phiazolidii	nediones	High	No	Gain	Potential benefit: plogilitazone	Increased risk	Low	Oral	Neutral	No dose adjustment required Generally not recommended in renal impaturent due to potential for fluid secention	FDA Black Box: Congestive heart failure (plogilitazone; ros/gilitazone) Fluid retention (edema; heart failure) Benefit in NASH Risk of boxe fractures Bladder cancer (plogilitazone) PLDL cholesterol (pos/gilitazone)
ielfonylur 2nd gener		High	Yes	Gain	Neutral	Neutral	Low	Oral	Neutral	Glyburide: not recommender Glyburide and glimepiride: initiate conservatively to avoid hypoglycemia	FDA Special Warning on increased risk of cardiovascular mortality based on studies of an older sulfonyfures (tolbutamide)
nsuffin	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
Analogs	1						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.



Figure 2

GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH TO AVOID CLINICAL INERTIA REASSESS AND EIRST-LINE THERAPY IS METFORMIN AND COMPREHENSIVE LIFESTYLE (INCLUDING WEIGHT MANAGEMENT AND PHYSICAL ACTIVITY) MODIFY TREATMENT IF HbA, ABOVE TARGET PROCEED AS BELOW REGULARLY NO **ESTABLISHED ASCVD OR CKD** WITHOUT ESTABLISHED ASCVD OR CKD ASCVD PREDOMINATES HF OR CKD PREDOMINATES COMPELLING NEED TO MINIMISE WEIGHT EITHER/ COMPELLING NEED TO MINIMISE HYPOGLYCAEMIA COST IS A MAJOR ISSUE9-10 **PREFERABLY** GAIN OR PROMOTE WEIGHT LOSS SGLT2i with evidence of reducing HF and/or CKD progression in CVOTs SGLT2i with GLP-1 RA with proven CVD if eGFR adequate3 proven CVD ---- OR -----GLP-1 RA benefit1. if eGFR benefit1 with good adequate2 If SGLT2i not tolerated or contraindicated DPP-4i GLP-1 RA SGLT2i² TZD SGLT2i² SU⁶ TZD10 or if eGFR less than adequate2 add GLP-1 efficacy for RA with proven CVD benefit¹ weight loss® If HbA_{1c} above target If HbA_{1c} above target If HbA, above target If HbA,, above target If HbA,, above target If HbA, above target If HbA_{1,} above target If HbA_{1c} above target GLP-1 RA SGLT2i² If further intensification is required or SGLT2i² SGLT2i² GLP-1 RA with good OR Avoid TZD in the setting of HF natient is now unable to tolerate DPP-4i DPP-4i SGLT2i² efficacy for weight TZD¹⁰ SU6 OR GLP-1 RA and/or SGLT2i, choose agents Choose agents demonstrating CV safety: TZD T7D OR OR loss8 demonstrating CV safety: · Consider adding the other class with GLP-1 RA TZD · Consider adding the other class (GLP-1 proven CVD benefit1 RA or SGLT2i) with proven CVD benefit DPP-4i (not saxagliptin) in the setting of DPP-4i if not on GLP-1 RA HF (if not on GLP-1 RA) If HbA, above target If HbA, above target If HbA, above target Basal insulin⁴ · Basal insulin⁴ TZD¹ • SU⁶ SU⁶ Continue with addition of other agents as outlined above Insulin therapy basal insulin with lowest If triple therapy required or SGLT2i and/or acquisition cost GLP-1 RA not tolerated or contraindicated use regimen with lowest risk of weight gain Consider DPP-4i OR SGLT2i with lowest 1. Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence of liraglutide > semaglutide > exenatide. For SGIT2i If HbA, above target PREFERABLY acquisition cost10 evidence modestly stronger for empagliflozin > canagliflozin. DPP-4i (if not on GLP-1 RA) Be aware that SGLT2i vary by region and individual agent with regard to indicated level of eGFR for initiation and continued use Both empagliflozin and canagliflozin have shown reduction in HF and reduction in CKD progression in CVOTs based on weight neutrality Consider the addition of SU⁶ OR basal insulin: Degludec or U100 glargine have demonstrated CVD safety Low dose may be better tolerated though less well studied for CVD effects Choose later generation SU with lower risk of risk of hypoglycaemia Choose later generation SU with lower risk of hypoglycaemia Consider basal insulin with lower risk of hypoglycaemia? Degludec / glargine U300 < glargine U100 / detemir < NPH insulin If DPP-4i not tolerated or contraindicated Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide or patient already on GLP-1 RA, cautious If no specific comorbidities (i.e. no established CVD, low risk of hypoglycaemia and lower priority to avoid weight gain or no weight related comorbidities) addition of: 10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and BPP-4i relatively cheaper • SU6 • TZD5 • Basal insulin



Figure 2

GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH CLINICAL INERTIA REASSESS AND FIRST-LINE THERAPY IS METFORMIN AND COMPREHENSIVE LIFESTYLE (INCLUDING WEIGHT MANAGEMENT AND PHYSICAL ACTIVITY) MODIFY TREATMENT REGULARLY IF HbA, ABOVE TARGET PROCEED AS BELOW NO ESTABLISHED ASCVD OR CKD **ASCVD PREDOMINATES** HF OR CKD PREDOMINATES **PREFERABLY** SGLT2i with evidence of reducing HF and/or CKD progression EITHER/ GLP-1 RA with proven SGLT2i with proven CVD in CVOTs if eGFR adequate3 OR CVD benefit1 benefit1, if eGFR adequate2 OR If SGLT2i not tolerated or contraindicated or if eGFR less than adequate² add GLP-1 RA with proven CVD benefit1 If HbA_{1c} above target If HbA_{1c} above target If further intensification is required or patient is now unable to tolerate · Avoid TZD in the setting of HF GLP-1 RA and/or SGLT2i, choose agents demonstrating CV safety: • Consider adding the other class (GLP-1 RA or SGLT2i) with proven CVD Choose agents demonstrating CV safety: benefit Consider adding the other class with proven CVD benefit¹ • DPP-4i if not on GLP-1 RA • DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1 RA) Basal insulin⁴ • Basal insulin4 1. Proven CVD evidence m TZD⁵ SU⁶ . Be aware th Both empac SU⁶ Degludec or Low dose m Choose late Degludec / glargine U300 < glargine U100 / deternir < NPH insulin If DPP-4i not tolerated or contraindicated 8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide or patient already on GLP-1 RA, cautious If no specific comorbidities (i.e. no established CVD, low risk of hypoglycaemia and lower priority to avoid weight gain or no weight related comorbidities addition of: 10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper • SU6 • TZD5 • Basal insulin



Effects of Newer DM Medications: MACE (Major Cardiovascular Events)

Drug Class	LEADER	REWIND	SUSTAIN-6*	EXSCEL
GLP-1 Long acting agonists	Beneficial	Beneficial	Beneficial	Neutral
	EMPA-REG	CANVAS	DECLARE	CREDENCE
SGLT2-Inhibitor				
	Beneficial	Beneficial	Neutral	Beneficial

MACE = Major Adverse Cardiovascular Events: CV death, MI, stroke.



^{*} Statistical testing for superiority not prespecified in SUSTAIN-6

Among patients with ASCVD in whom HF coexists or is of concern, SGLT2 inhibitor are recommended

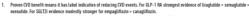
Rationale: Patients with T2D are at increased risk for heart failure with reduced or preserved ejection fraction

Significant, consistent reductions in hospitalization for heart failure have been seen in SGLT2 inhibitor trials

Caveat: trials were not designed to adjudicate heart failure

Majority of patients did not have clinical heart failure at baseline

PREFERABLY SGLT2i with evidence of reducing HF and/or CKD progression in CVOTs if eGFR adequate³ OR If SGLT2i not tolerated or contraindicated or if eGFR less than adequate² add GLP-1 RA with proven CVD benefit¹ If HbA_{1c} above target • Avoid TZD in the setting of HF Choose agents demonstrating CV safety: • Consider adding the other class with proven CVD benefit¹ • DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1 RA) • Basal insulin⁴ • SU⁴



- 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
- Low dose may be better tolerated though less well studied for CVD effects
 Choose later generation SU with lower risk of hypodycaemia



Effects of Newer DM Medications: Heart Failure

Drug Class	LEADER	REWIND	SUSTAIN-6*	EXSCEL
GLP-1 Long acting agonists	Neutral	utral Neutral Ne		Neutral
	EMPA-REG	CANVAS	DECLARE	CREDENCE
SGLT2-Inhibitor	EMPA-REG	CANVAS	DECLARE	CREDENCE

MACE = Major Adverse Cardiovascular Events: CV death, MI, stroke.



^{*} Statistical testing for superiority not prespecified in SUSTAIN-6

CHOOSING GLUCOSE-LOWERING MEDICATION IN THOSE WITH ESTABLISHED HF OR CKD

PREFERABLY SGLT2i with evidence of reducing HF and/or CKD progression in CVOTs if eGFR adequate³ OR If SGLT2i not tolerated or contraindicated or if eGFR less than adequate² add GLP-1 RA with proven CVD benefit¹ If HbA_{1c} above target • Avoid TZD in the setting of HF Choose agents demonstrating CV safety: • Consider adding the other class with proven CVD benefit¹ • DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1 RA) • Basal insulin⁴ • SU⁴

- Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence of tiragilutide > semaglutide > exenatide. 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
- Both empagliflozin and canagliflozin have shown reduction in HF and reduction in CXO progression in CXOTs
- 4. Degludec or U100 glargine have demonstrated CVD safety
- Low dose may be better tolerated though less well studied for CVD effects
 Choose later generation SU with lower risk of hypoglycaemia





Figure 2 GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH TO AVOID
CLINICAL INERTIA
REASSESS AND
MODIFY TREATMENT
REGULARLY FIRST-LINE THERAPY IS METFORMIN AND COMPREHENSIVE LIFESTYLE (INCLUDING WEIGHT MANAGEMENT AND PHYSICAL ACTIVITY) IF HbA, ABOVE TARGET PROCEED AS BELOW NO **ESTABLISHED ASCVD OR CKD** WITHOUT ESTABLISHED ASCVD OR CKD ASCVD PREDOMINATES HF OR CKD PREDOMINATES COMPELLING NEED TO MINIMISE WEIGHT COMPELLING NEED TO MINIMISE HYPOGLYCAEMIA **COST IS A MAJOR ISSUE⁹⁻¹⁰** DPP-4i TZD SU⁶ TZD^{10} If HbA_{1c} above target If HbA_{1c} above target SGLT2i2 OR TZD SGLT2i² **OR** DPP-4i **OR** GLP-1 RA If HbA_{1c} above target TZD¹⁰ SU⁶ eviden 2. Be awa 3. Both e If HbA_{1c} above target Consider the addition of SU⁶ C • Insulin therapy basal insulin with lowest acquisition cost • Choose later generation SU OR • Consider basal insulin with

• Consider DPP-4i OR SGLT2i with lowest acquisition cost10



Diabetes Medications Can Be Costly

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



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

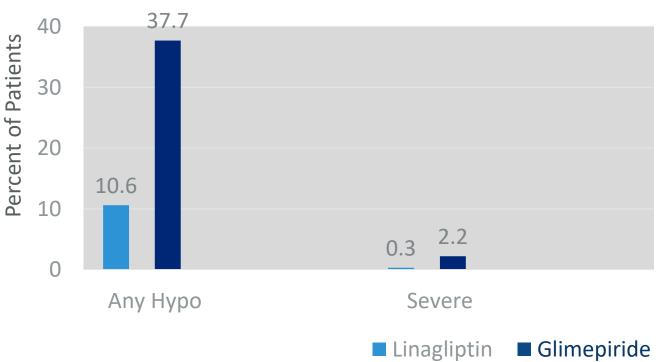
- Results:
 - No difference in primary outcome with HR 0.98 (95% CI 0.84-1.14)
 - No difference in CV morality (HR = 1.0)
 - No difference in A1C (glimepiride lower early but higher later)
 - 1.5 Kg lower weight with linagliptin
 - Much lower hypoglycemia with linagliptin



CAROLINA Study

- Linagliptin vs Glimepiride -

Hypoglycemia





Summary of ADA/EASD Consensus on T2DM Management

- It is important to have a patient centered approach
 - Shared decision making
 - Diabetes education is important periodically
- Metformin and lifestyle change are the foundation therapy for all patients.
- When the A1C no longer reaches the individual's goal, consider the cardiovascular and renal status
 - GLP-1 RA or SGLT2 inh if CVD is present
 - Prefer SGLT2 inh if HF or kidney disease are present
- Specific patient characteristics and circumstances guide therapy when heart disease is not a factor.
- GLP-1 RA are preferred as first injectable and before prandial insulin if patient is on basal insulin



Medication Adherence in Diabetes

- Varies with population but 35-45% of patient 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



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
- Diabetes distress



Summary

- Effective diabetes management requires a team effort and an evidence-based approach
- The patient is the key member of the team
- Success requires a comprehensive approach that includes glucose control but also improved health habits, prevention of cardiovascular disease, enhanced patient understanding of their disease, and complication surveillance and treatment.
- Adherence to lifestyle changes and medical treatment is a major problem that requires system attention
- Behavioral services are critical to success for many patients.





Thank you!

This webinar is a service of the Oregon Health Authority Transformation Center.

- For more information about this presentation, contact <u>Transformation.Center@state.or.us</u>
- 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

