The Diabetes Balancing Act – What to Keep, What to Let Go

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Learning Objectives

- Identify goals of therapy for diabetes care for patients in hospice
- List medications for type 2 diabetes
- Develop a patient care plan for medications for type 2 diabetes

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DM2 in the US

Incidence

- 37.3 million (11.3% of population) people have diabetes
- 90-95% of patients with diabetes have type 2 diabetes (DM2)

People with diabetes account for $1 of every $4 spent in US health care

CDC 2021; CDC 2022; ADA 2023

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DM2: Cost to Hospice

2022 data hospice pharmacy claims database

- $2.5M in claims for antidiabetic medications
- About 1% of total claims

Drop in the bucket of diabetes meds cost in US

- $15B for insulins
- $15.9B for non-insulin diabetes meds
- $71.2B for excess use of meds due to DM co-morbidities

Optum 2023; ADA 2023

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DM2: Cost to Hospice

Top 10 Meds/Total Claims*

Diabetes Med	Claims Count
METFORMIN	12,431
INSULIN GLARGINE	3,865
GLIPIZIDE	3,709
GLIMEPIRIDE	2,287
INSULIN LISPRO	1,780
INSULIN ASPART	1,331
JANUVIA	1,159
INSULIN REGULAR	1,117
PIOGLITAZONE	601
INSULIN NPH	561

*National hospice PBM claims data

Top 10 Meds/Total Cost*

Diabetes Med	Total Cost
INSULIN GLARGINE	$593,983
JANUVIA	$302,014
INSULIN ASPART	$230,352
INSULIN LISPRO	$199,226
JARDIANCE	$150,198
TRADJENTA	$126,278
LEVEMIR	$118,182
METFORMIN	$114,859
FARXIGA	$97,546
INSULIN REGULAR	$95,656

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DM2: Complications

- Vision – diabetic retinopathy
  - Leading cause of blindness in adults 20-74 years
  - Risk increases with duration of DM and uncontrolled hyperglycemia
- Kidneys – renal insufficiency
  - Diabetic kidney disease estimated 20-40% of people with DM
  - May be present at diagnosis for DM2
  - Leading cause of ESRD in US
- Skin – impaired wound healing, complex infections (diabetic foot ulcers)

ADA 2023

DM2: Complications

- Neuropathies
  - Autonomic – orthostatic hypotension, syncope, resting tachycardia, dry/cracked skin (indicator of poor circulation)
  - Gastrointestinal – gastroparesis, constipation, diarrhea
  - Peripheral - numbness, tingling, burning, loss of protective sensation

- Plus obesity, cardiovascular disease, dementia, depression

Coverage and Relatedness

- "…Coverage under the Medicare Hospice benefit requires that hospice services must be reasonable and necessary for the palliation and management of the terminal illness and related conditions..." (CMS, 2022)
- "…hospices are required to provide virtually all the care that is needed by terminally ill patients… law allows for circumstances in which services needed by a hospice beneficiary would be completely unrelated to the terminal illness and related conditions, but we believe… rare exception rather than the norm…hospice coverage of drugs was very broad and very inclusive… Part D payment for drugs furnished to hospice beneficiaries would be rare…" (CMS, 2014)

CMS 2022; CMS 2014

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Patient Case- Henry

Henry is an 82-year-old with a primary hospice diagnosis of hypertensive heart and chronic kidney disease with heart failure with a past medical history significant for DM2. In addition to his cardiac medications, Henry has the following medications to treat diabetes:

- Metformin 1000 mg PO BID
- Januvia (sitagliptin) 50 mg PO daily
- Glipizide 5 mg PO daily
- Farxiga (dapagliflozin) 10 mg PO daily

His blood glucose at last check was 190 mg/dL

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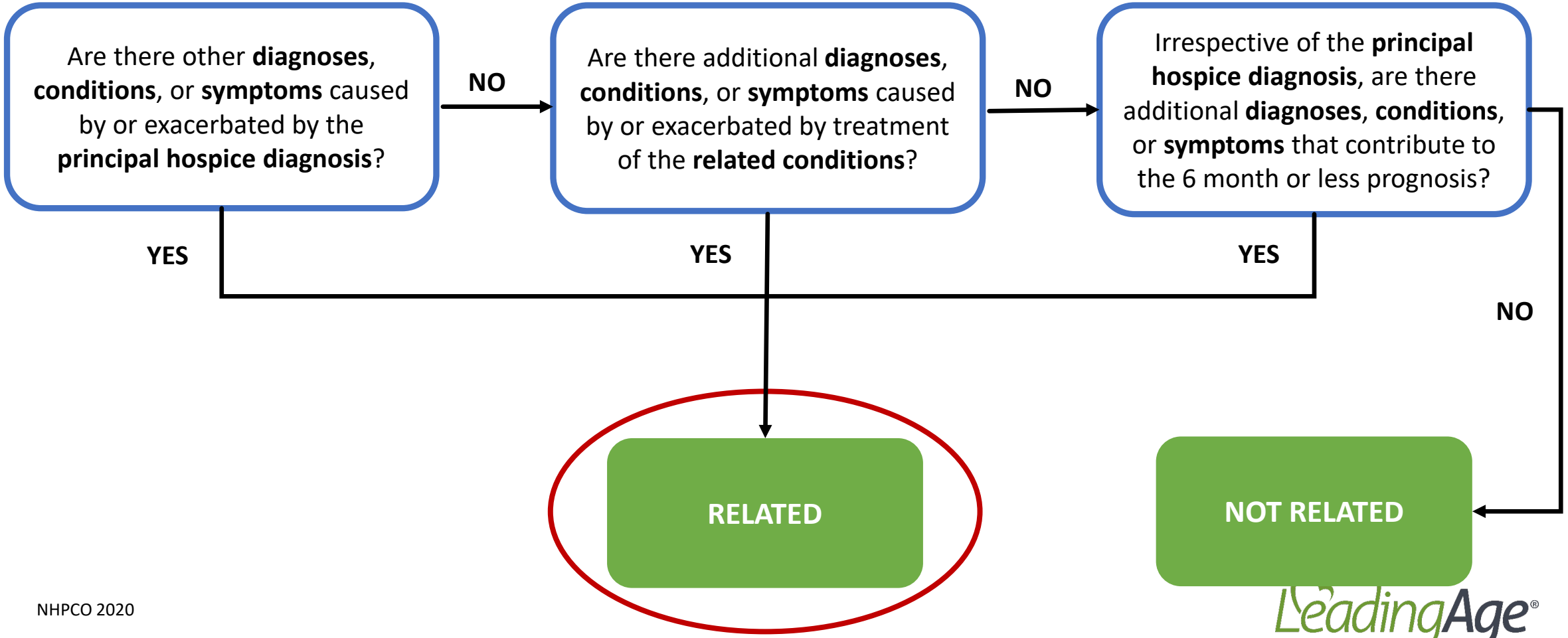
Determining Relatedness



NHPCO 2020

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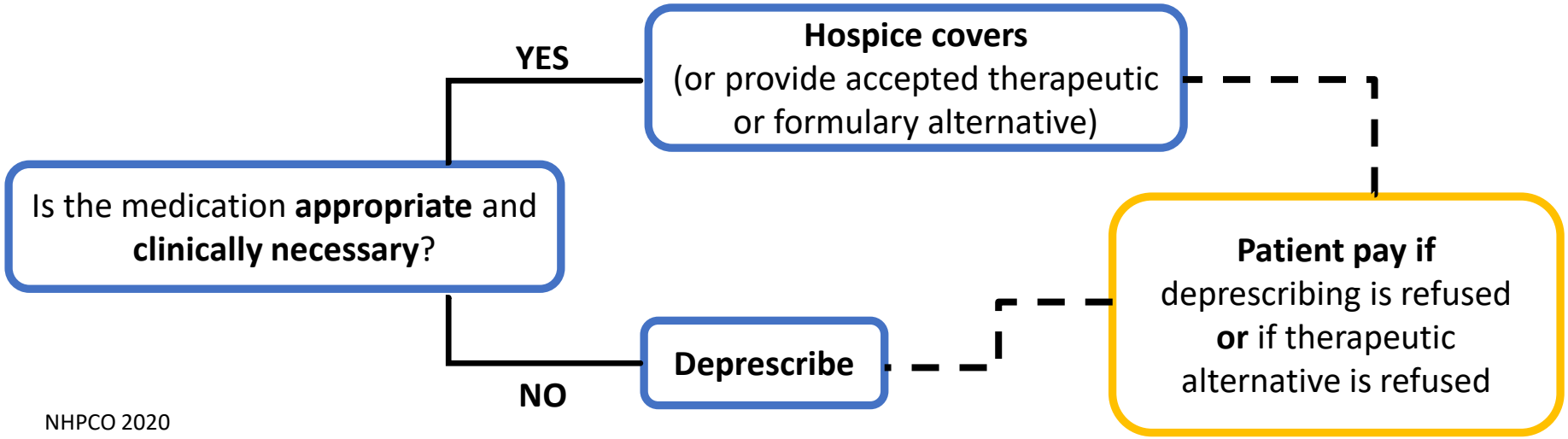
Coverage and Relatedness

The decision about relatedness and coverage is determined by the hospice physician in collaboration with the hospice team and is individualized based on the patient's clinical status

- Patient-by-patient
- Case-by-case



NHPCO 2020

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Goals of Care

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DM2 Management in Hospice

Goals of Care - avoid hypoglycemia and symptomatic hyperglycemia

- Reduce burden of diabetes management
- Glucose targets prevent hypoglycemia and hyperglycemia
- Treatment interventions focus on QOL
- Blood glucose goal 150-250 mg/dL prevents symptoms
- A1C testing is unlikely to be beneficial

Poulson 1997; Tice 2006; Zylic 2010; Jeffreys 2015; ADA 2023

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Symptoms of Hypo- and Hyperglycemia

Hypoglycemia
- Diaphoresis
- Anxiety
- Tremors
- Weakness
- Irritability
- Palpitations
- Seizures

Hyperglycemia
- Thirst
- Increased urination
- Blurred vision
- Dehydration
- Dizziness
- Malaise
- Agitation

May mimic signs and symptoms of impending death – always consider checking blood glucose

Hypoglycemia

Regularly assess patients for symptoms of hypoglycemia

- Elderly patients, frail, hospice patients → hypoglycemia unawareness

DM2 in LTC residents receiving hospice care

- 10% experienced hypoglycemia
- 33% if taking insulin

Optum 2022; Petrillo 2018

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Hyperglycemia

Increased risk

- Urinary tract infection
- Candidiasis
- Impaired wound healing

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Blood Glucose Monitoring for DM2

Depends on current medications and prognosis

- Fingerstick testing

  Prognosis = months

  - Oral antidiabetic meds and low risk of hypo- or hyperglycemia?
    - May only need to check if experiencing symptoms
  - All patients taking insulin must continue blood glucose monitoring

  Prognosis < 1 week

  - Discontinue fingerstick testing
  - Discontinue diabetes medications (orals and insulins)

Jeffreys 2015; Ford-Dunn 2006

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Medication Classes

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DM2 General Treatment Strategy

First Line: Oral med selection based on comorbidities, patient-centered treatment factors, cost and access

Next: Add oral or non-insulin injectable meds to achieve and maintain glycemic goals

Next: If glycemic goal still not achieved, consider add non-insulin injectable or other oral med class

Next: Add insulin starting with basal insulin

ADA 2023

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DM2 Oral Medications

Alpha-glucosidase Inhibitors	DPP-4 Inhibitors	GLP-1 Agonists	Meglitinides
Acarbose (Precose) Miglitol (Glyset)	Alogliptin (Nesina)+ Linagliptin (Tradjenta)+ Saxagliptin (Onglyza)+ Sitagliptin (Januvia)+	Semaglutide++ (Rybelsus)	Nateglinide (Starlix) Repaglinide (Prandin)+
SGLT2 Inhibitors	**Sulfonylureas**	**Thiazolidinediones**	**Biguanide**
Canagliflozin (Invokana)+ Dapagliflozin (Farxiga)+ Empagliflozin (Jardiance)+ Ertugliflozin (Steglatro) Bexagliflozin (Brenzavvy) Sotagliflozin (Inpefa)	Glimepiride+ Glipizide+ Glyburide+	Pioglitazone (Actos)+	Metformin+

+ also available in combo products
++ also available as injectable Ozempic (semaglutide)

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Focused discussion on SGLT2 Inhibitors …*not just for diabetes anymore?*

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Cardiovascular – SGLT2 Inhibitors

Inhibit SGLT2 to reduce resorption of glucose in renal proximal tubule... increases urinary glucose excretion.

	DM2	CV-HF	CKD
Brenzavvy (bexagliflozin)	✓		
Farxiga (dapagliflozin)	✓	✓	✓
Inpefa (sotagliflozin)	✓	✓	
Invokana (canagliflozin)	✓		
Jardiance (empagliflozin)	✓	✓	
Steglatro (ertugliflozin)	✓		

DM2: diabetes type 2 CV-HF: cardiovascular-heart failure CKD: chronic kidney disease

LexiComp, 2023; Heidenreich et al, 2022

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Cardiovascular – SGLT2 Inhibitors

Farxiga (dapagliflozin)	Jardiance (empagliflozin)	Inpefa (sotagliflozin)
• Risk reduction for CV mortality, HF hospitalization • Risk reduction eGFR decline, ESRD, CV death/hospitalization for heart failure in CKD	• Risk reduction for CV mortality, HF hospitalization	• Risk reduction for CV mortality, HF hospitalization
10mg PO Daily	10mg PO Daily	200mg PO daily titrate to 400mg if tolerated, within 1 hour of first meal of day
Avoid use or stop if CrCL < 20-25 mL/min. All are contraindicated for patients on dialysis		
10mg tab: $22.60 each	• 10mg tab: $23.75 each	200mg tab: $23.95 each

All SGLT2 Inhibitors

Increased risk of UTI and genital yeast infection, hypovolemia, hypotension, syncope, dehydration

LexiComp, 2023

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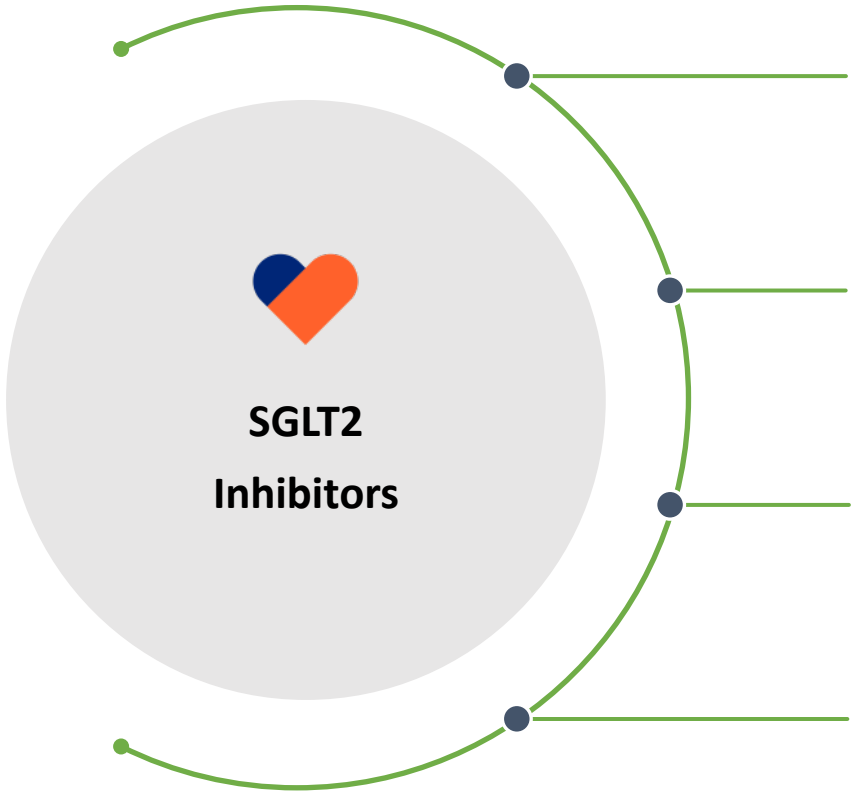
Cardiovascular – SGLT2 Inhibitors



RISK: Urinary tract & genital fungal infections

- Comorbid diabetes
- History of UTI or genital fungal infections
- Women, uncircumcised men

RISK: Hypovolemia & dehydration

- Age > 75 years; CrCL < 60 mL/min; reduced oral intake
- Use with blood pressure meds or diuretics; preexisting low systolic BP

RISK: Limited clinical trial data for older adults

- No hospice/palliative care patients in clinical trials, with only 6% > 75 years
- Risk reduction doesn't really start for 2.5-5 years of use

RISK: Polypharmacy & drug interactions

- Patients should already be on ACE inhibitor/ARB, beta-blocker, and aldosterone antagonist in addition to the SGLT2 increasing polypharmacy, adverse drug events, medication adherence concerns, and drug interaction risk.

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LexiComp, 2023; Elsayed et al, 2023

DM2 Non-Insulin Injectables

GLP-1 Agonists	GLP-1 + GIP Agonist	Amylin Analog
Dulaglutide (Trulicity) Exenatide (Byetta, Bydureon) Liraglutide (Victoza)++ Lixisenatide (Adlyxin)++ Semaglutide (Ozempic) +	Tirzepatide (Mounjaro)	Pramlintide (SymlinPen)

++ also in combo injections – liraglutide/insulin degludec (Xultophy); lixisenatide/insulin glargine (Soliqua)
+ also available as oral Rybelsus (semaglutide)

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DM2 Insulins & Biosimilars

Rapid-Acting	Short/Regular/Intermediate
Insulin aspart (Novolog, ReliOn, Fiasp) Insulin lispro (Humalog, Admelog, Lyumjev-aabc) Insulin glulisine (Apidra)	Insulin regular (Novolin R, Humulin R) Insulin NPH (Novolin N, Humulin N)
Long-Acting	
Insulin glargine (Lantus, Semglee, glargine-yfgn, Rezvoglar, Basaglar, Toujeo) Insulin degludec (Tresiba) Insulin detemir (Levemir)	
Mixed	
Insulin NPH+R (Humulin 70/30, Novolin 70/30) Insulin lispro protamine + lispro (Humalog Mix 50/50 or 75/25) Insulin aspart protamine + aspart (Novolog Mix 70/30) Insulin glargine + lixisenatide (Xultophy) Insulin degludec + liraglutide (Soliqua)	

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Cost of Long-Acting Insulins

Least Expensive → 3mL pen 100 units/mL →							**Most Expensive**
Rezvoglar Insulin glargine	Insulin glargine-yfgn	Insulin degludec	Basaglar Insulin glargine	Semglee-yfgn Insulin glargine-yfgn	Lantus Insulin glargine	Levemir Insulin detemir	Tresiba Insulin degludec
$22	$37	$43	$78	$97	$106	$111	$122

Lexi 2023

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Cost of Rapid-Acting Insulins

Least Expensive →		Rapid-Acting 3mL pen 100 units/mL		→ Most Expensive	
Insulin lispro	Admelog Insulin lispro	Insulin aspart	Humalog, Lyumjev Insulin lispro	Apidra Insulin glulisine	Novolog, Fiasp Insulin aspart
$38	$45	$67	$127	$132	$134

Lexi 2023

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Converting Between Insulin Doses

Conversion is not always on a unit-per-unit basis

- Consult with a clinical pharmacist for dosing recommendations
- Ensure proper patient education with any changes of insulins
  - Especially if changing between pens and vials
  - Avoid duplications of therapy
  - Check insulin expiration dates and storage conditions

Patient Case – Henry

Henry is 82 years old with a primary hospice diagnosis of hypertensive heart and chronic kidney disease with heart failure. He has DM2 and his blood glucose at last check was 190 mg/dL. His diabetes meds are

- metformin 1000 mg PO BID
- Januvia (sitagliptin) 50 mg PO daily
- glipizide 5 mg PO daily
- Farxiga (dapagliflozin) 10 mg PO daily

Which of Henry's medications has highest risk of hypoglycemia?

A. Metformin

B. Sitagliptin

C. Glipizide

D. Empagliflozin

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Decision Making on Discontinuing Medications

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Treatment Approach to DM2 in Hospice

Months to > 1 Year

Goal: prevent hypoglycemia and symptomatic hyperglycemia

Adjust medications for

- Nausea/vomiting
- Hepatic/renal impairment
- Decreased oral intake
- Hypoglycemia

Start deprescribing conversations

Days to Weeks

Goal: prevent hypoglycemia

Adjust medications for

- Adverse effects
- Decreased oral intake
- Hypoglycemia

Consider discontinuation of finger-stick glucose checks if no insulin used

Start deprescribing

Hours to Days

Goal: patient comfort

Discontinue any remaining DM2 medications

Angelo 2010; Jeffreys 2015; Optum 2022

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Diabetes Medications Overview

	Metformin	Sulfonylureas	TZDs	DPP-4 Inhibitors	SGLT2 Inhibitors	GLP-1 RA	Basal Insulin
Hypoglycemia Risk	Low	Moderate-High	Low	Low	Low	Low	Moderate-High
Adverse Effects	GI, Lactic acidosis	Hypoglycemia	Edema HF Fractures	Rare	Dehydration, UTI, genital candidiasis	GI, weight loss	Hypoglycemia
Cost	Low	Low	Low	High	High	High	Moderate-High

Optum 2022; Lexi 2023

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Assessing Patient Response

Routinely assess and document patient's response to diabetes medications to help determine need for deprescribing

- On admission to hospice
- With any exacerbation of condition
- With a decline in status
- At every recertification
- Prior to ordering medication refills
- With every change in location (transition of care)

Optum 2022

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Considerations for Med Discontinuation

- Patient and family wishes
- Recent blood glucose levels
- Patient prognosis
- Side effects
- Organ function
- Comorbidities and other medications
- Ease of admin and monitoring
  - Is patient able to check blood glucose?
  - Is patient about to administer injectable medications?
- Immediate efficacy at lowering blood glucose
- Cost

Patient Case – Sarah

Sarah is 79 years old with a primary hospice diagnosis of lung cancer. Her past medical history includes stage IV CKD (CrCL 15-29 mL/min) and she has DM2 and her blood glucose at last check was 150 mg/dL. She's like to take fewer medications and is concerned about her kidneys.

Her current diabetes medications include

- metformin 1000 mg PO BID
- insulin glargine-yfgn ("Lantus") 20 units daily
- glipizide 5 mg PO daily

Which of the following is the most appropriate to deprescribe at this time?

A

Metformin; eGFR < 30 mL/min and use is contraindicated

B

Glipizide; high risk of hypoglycemia

C

Insulin glargine-yfgn; costly and not appropriate in hospice

D

Both metformin and glipizide

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Patient Case – Sarah

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Safe Use of Insulins

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Strategies for Improving Insulin Safety

Risk	Strategies to Reduce Risk
Errors with Insulin Ordering	• Avoid orders with trailing zeros (**never** 10.0 units) • Use “units” instead of abbreviating with “U” or “u” • Use TALLman lettering to prevent mix-ups with look-alike drug names (e.g., HumuLIN and HumaLOG) • Specify packaging (pens, vials, cartridges) • Confirm product patient currently using

ISMP 2023; Lexi 2023; Optum 2022

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Strategies for Improving Insulin Safety

Risk	Strategies to Reduce Risk
Confusion between Insulin Products	• Be aware of potential look-alike and sound-alike confusion when ordering insulin • Educate patients/caregivers about insulin products • Encourage patients/caregivers to double-check they are using the correct pen or vial prior to administration

ISMP 2023; Lexi 2023; Optum 2022

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Strategies for Improving Insulin Safety

Risk	Strategies to Reduce Risk
Improper Storage	• Store insulin in refrigerator prior to use • Once opened, label the insulin pen or vial with beyond use date. • Most products are stable at room temp for 28 days after opening • Expired insulin reduces effectiveness and potency • Advise patients/caregivers to check expiration dates

ISMP 2023; Lexi 2023; Optum 2022

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Treatment of Hypoglycemia

Conscious Patient	Unconscious Patient
Blood glucose < 70 mg/dL	
• *Preferred*: Glucose (15-20g) • Alternative: Quick sugar foods • Check BG 15 mins after treatment; if blood glucose remains < 70 mg/dL, repeat treatment	• Treat with glucagon product (injection or intranasal) • Administer oral glucose as soon as possible after patient is alert enough for oral intake

ADA 2023; Optum 2022

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Glucagon Products

Product	Dosing	Route	Cost
Glucagon recons soln, injection (GlucaGen HypoKit, Glucagon Emergency)	1 mg; may repeat in 15 mins PRN	IM IV SC	GlucaGen® HypoKit® 1mg: $369 Glucagon Emergency Inj 1mg: $206
Glucagon nasal powder (Baqsimi)	3 mg into one nostril; may repeat in 15 mins (new device)	IN	Baqsimi® 1Pack Nasal 3mg: $337 Baqsimi® 2Pack Nasal 3mg: $674
Glucagon prefilled syringe (Gvoke PFS, HypoPen)	1 mg; may repeat in 15 mins PRN (new device)	SC	Gvoke® PFS 1mg/0.2mL: $368 Gvoke HypoPen® 1mg/0.2mL $368

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When to Discontinue Insulin?

- Patient no longer wants to check blood glucose
- Patient or caregiver - difficulty or errors with insulin administration
- Reduced food intake
- Hypoglycemic episodes

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Session Key Points

- Strict blood glucose control not appropriate for most hospice patients
- ADA recommends blood glucose of < 200 mg/dL to prevent symptoms of hypo- and hyperglycemia in frail, older adults with limited life expectancy
- Routinely assess patient's diabetes medication regimen
  - look for opportunities to lower medication and monitoring burden
- Evaluate patient for adverse effects and hypoglycemia risk

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QUESTIONS?

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