Management of Hyperglycemia in Hospitalized Adult Patients in Non-Critical Care Settings: An Endocrine Society 2022 Clinical Practice Guideline

(and beyond)

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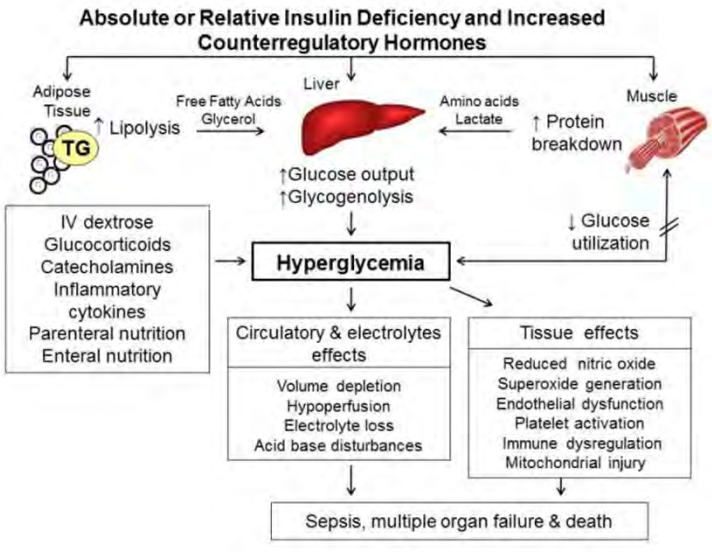
Stats ….

- US: > 10 % of the population, have diabetes
- 3-fold greater chance of hospitalization
- HG/DM > 30 % of noncritically ill hospitalized patients
- Hypo and hyperglycemia associated w increased morbidity and mortality



Dhatariya et al Endotext

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Many questions remain unanswered

- **Management of Hyperglycemia in Hospitalized Adult Patients in Non-Critical Care Settings: An Endocrine Society Clinical Practice Guideline**
  JCEM | August 2022
- Mary T. Korytkowski (Chair), Ranganath Muniyappa (Co-Chair), Kellie Antinori-Lent, Amy C. Donihi, Andjela T. Drincic, Irl B. Hirsch, Anton Luger, Marie E. McDonnell, M. Hassan Murad, Craig Nielsen, Claire Pegg, Robert J. Rushakoff, Nancy Santesso, Guillermo E. Umpierrez

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Question 1. CGM (w confirmatory POC) for adjustments in insulin dosing) vs bedside POC

In adults with insulin-treated DM at high risk of hypoglycemia, we suggest the use of real-time CGM with confirmatory POC-BG monitoring for adjustments in insulin dosing rather than POC-BG testing alone in hospital settings where resources and training are available. (2⊕⊕◯◯)

- In hospitals where CGM is not available, POC-BG is an alternative

- high risk for hypoglycemia:
- age ≥65 years;
- BMI ≤27 kg/m^2;
- Insulin TDD ≥0.6 units/kg;
- eGFR < 60 mL/min/1.73m^2,
- liver failure
- cerebrovascular accident,
- active malignancy
- pancreatic disorders
- congestive heart failure
- infection
- history of preadmission hypoglycemia or hypoglycemia occurring during a recent or current hospitalization; or impaired awareness of hypoglycemia.

rec does not apply to situations in which CGM may not be accurate

- extensive skin infections
- hypoperfusion, or hypovolemia or
- those receiving vasoactive or pressor therapy
- some medications can cause inaccurate CGM readings (e.g., acetaminophen >4 g/day, dopamine, vitamin C, hydroxyurea)

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Q1: CGM

- 5 RCTs and 4 non-RCTs
- evidence is uncertain
- CGM may increase the detection of hypoglycemic events
- reduces the percentage of time with BG > 180 mg/dL
- Three RCTs demonstrated reductions in time spent in hypoglycemia compared to POC-BG testing
- 4 RCTs demonstrated reductions in mean daily BG for ~ 15 mg/dl

- Accuracy of CGM devices when compared to POC-BG in inpatient setting is moderate to good
- Lower accuracy of CGM for BG < 70 mg/dL raises concern for overtreating low BG;
- Lower accuracy at higher BG supports rec to confirm results with POC-BG for insulin adjustments
- Calibration of any CGM device with POC-BG within the first 12 hours following initial placement of the sensor device is important for validating the reliability
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Q1: CGM

Table 2.

Resources required for safe implementation of continuous glucose monitoring in the noncritical care hospital setting

Engagement, training, and education of nursing personnel
Patient education regarding care of the device and how to respond to alarms for high or low BG
Purchase of equipment (eg, sensors, transmitters, receivers)
Expertise from healthcare professionals knowledgeable in this technology
Oversight and guidance for CGM use
Integration of CGM data with the hospital electronic medical record
Clarity of assigned responsibility for interpreting and acting on CGM data

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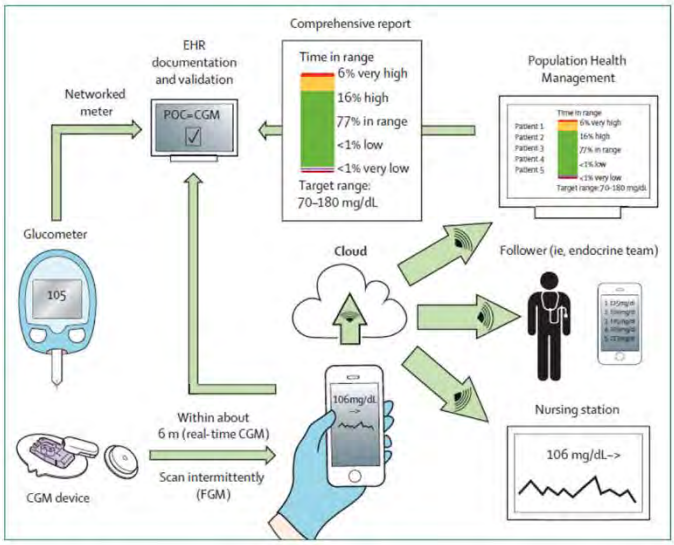
Q1: CGM



- LSingh… E Spinakis Continuous Glucose Monitoring in General Wards for Prevention of Hypoglycemia: Diabetes Sci Technol 2020 Jul;14(4):783-790
- Fortmann, Philis-Tsimikas A Randomized Controlled Trial of CGM in a Non-ICU Hospital Setting Diabetes Care 2020;43:2873–2877

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*Q2: Should **NPH** **vs basal bolus** insulin regimens be used for adults with hyperglycemia (with and without known diabetes) receiving **glucocorticoids**?*

- HG: 56% to 86% of hospitalized pts on supraphysiologic GCs
- GC-associated HG independent of preexisting diabetes, is associated with increased risk of mortality, cardiovascular events, and infections

- We suggest glycemic management with either NPH-based insulin or BBI regimens (2⊕⊕◯◯)
- NPH-based regimen may consist of NPH (with or without prandial insulin) given in divided doses depending on the timing, pharmacokinetics, and frequency of the specific GC being administered
- NPH may be added to BBI if the patient is already on this regimen.

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Q2: why ?

- Systematic review: 6 RCTs and 1 non-RCT
- Much variability occurred among the studies regarding the insulin regimens used
- doses of GCs ranged from 10 to 100 mg of prednisone equivalency administered with a frequency of 1 to 3 times a day
- Pts on GC require a higher per-centage of nutritional insulin to achieve normoglycemia
- Although experts commonly recommend that pharmacodynamic profiles of insulin should be reconciled ("matched") with corresponding profile of GCs, this has not been well-studied in the literature

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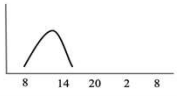
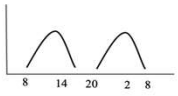
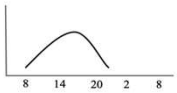
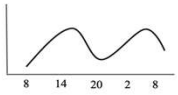
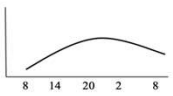
Table 1. Different corticosteroids and their equivalent doses, steroidal kinetics and potential to trigger hyperglycaemia.

Glucocorticoids		Approximate Equivalent Dose (mg)	Plasma Peak Concentration (minutes)	Elimination Half-Life (hours)	Duration of Action (hours)	Hyperglycaemic Effects (hours)		
						Onset	Peak	Resolution
Short-acting	Hydrocortisone	20	10	2	8–12	1	3	6
Intermediate-acting	Predniso(lo)ne	5	60–180	2.5	12–36	4	8	12–16
	Methylprednisolone	4	60	2.5	12–36	4	8	12–16
Long-acting	Dexamethasone	0.75	60–120	4	36–72	8	variable	24–36

Glucocorticoids		Hyperglycaemic Effects (hours)			Glucose Profiles (GC Given Once Daily [8 a.m.])	Glucose Profiles (GC Given Twice Daily [8 a.m. and 20 p.m.])
		Onset	Peak	Resolution		
Short-acting	Hydrocortisone	1	3	6		
Intermediate-acting	Predniso(lo)ne	4	8	12–16		
	Methylprednisolone	4	8	12–16		
Long-acting	Dexamethasone	8	variable	24–36		n.a.

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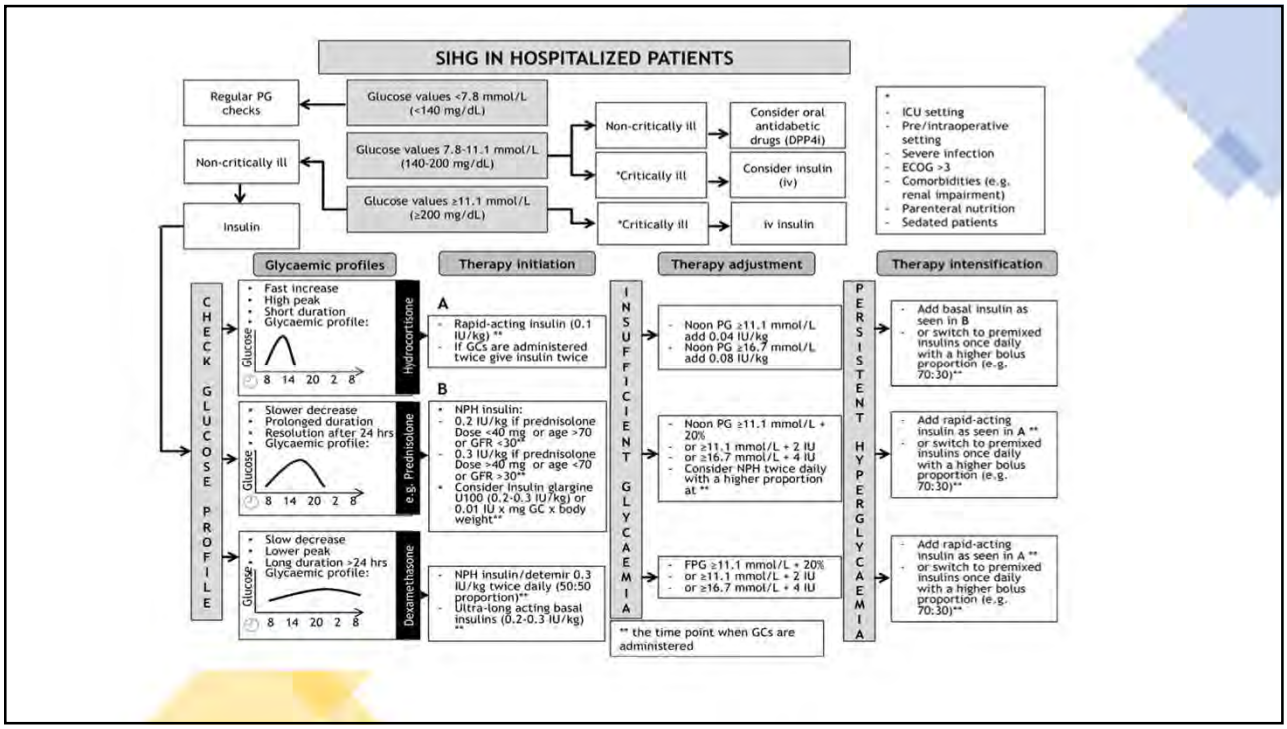

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Q 3:
*Should **insulin pump** therapy be continued vs transitioning to **SC BBI** for adults with diabetes on pump therapy who are hospitalized for noncritical illness?*

- 2 non-RCTs to addressed this question ; lower hypo
- We suggest that these patients continue insulin pump therapy rather than changing to SC BBI therapy in hospitals with access to personnel with expertise in insulin pump therapy
- Where expertise is not accessible, we suggest that patients with anticipated LOS > 1 to 2 days be transitioned to SC BBI before discontinuation of an insulin pump. (2⊕⊕◯◯)
- Not indicated for
  - impaired LOC
  - inability to appropriately adjust pump settings
  - ICU, DKA, HHS
- Availability of supplies is necessary
- Adaptation of the basal rate may be needed at time of admission.

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Q3: Methodology for converting continuous subcutaneous insulin infusion to scheduled basal bolus insulin

	Dosing suggestions[a]	
	Basal insulin dose	Prandial and/or correctional insulin dose[b]
Basal rate settings on pump known	Refer to the pump's active basal profile to determine the 24-hour basal insulin dose. Administer this dose as glargine U100 insulin as a single daily dose or in equally divided doses administered every 12 hours.	For patients who perform CC at home, allow patients to continue using the settings provided in the pump's active insulin profile for prandial and correctional insulin dosing. For patients not using CC, use weight-based fixed premeal insulin doses (0.2 to 0.4 units/kg divided into 3 prandial insulin doses with correctional insulin administered for BG above target range. For patients who are not eating, hold prandial insulin and continue correctional insulin dosing.
Basal rate settings on pump not known	Calculate basal insulin dose of 0.2 to 0.4 units/kg per day administered as glargine U100 given as a single daily dose or in equally divided doses administered every 12 hours.	Use weight-based fixed premeal insulin doses (0.2 to 0.4 units/kg divided into 3 prandial insulin doses). Hold if patient is not eating.

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Q3: pump vs BBI- hybrid closed-loop

Pts on hybrid closed-loop insulin pump therapy may be able to continue if they meet safe –pump criteria

If CGM fails or is removed from the patient, the insulin pump can be reverted to manual mode

Hospitals need policies, procedures including patients' informed consent, and standardized order sets in place as well as expertise from HCPs knowledgeable in pump therapy

Including information for pump management during MRI, CT, surgery

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Q 4.
*Should **inpatient diabetes education** be provided before discharge*

- 4 RCTs and 6 non-RCTs addressed this question
  - likely re- duces hemoglobin A1c (HbA1c) at 3 months by 1.25%
  - moderate benefit in readmission rates
  - may increase patient satisfaction
- we suggest providing inpatient diabetes education- comprehensive discharge-planning
- education is best provided by DCESs
  - DCESs can serve as a resource to other HCP to provide inpatient diabetes education (eg, staff nurses, pharmacists, dieticians, etc.) by providing training and support
  - DCESs should be Certified and/or hold the Board Certified-Advanced Diabetes Management credentials or be working toward 1 of these certifications

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Q 4: education

Comprehensive diabetes discharge-planning process

- education on diabetes survival skills
- referral for outpatient DSMES,
- scheduling DM f/u,
- ensuring access to the medications and supplies
- prioritize education for pts
  - at high risk for hospital readmission
  - admitted for diabetes-related issues
  - newly diagnosed with diabetes
  - newly starting insulin

survival skill education

- Teaching how to take/administer medications, including, but not limited to, insulin
- BG monitoring including when to test and goals of treatment
- Basic meal planning
- Prevention, identification, and treatment of hypoglycemia and hyperglycemia
- Who to contact for emergent questions or concerns
- following hospital discharge

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Q5.
*Should prespecified **preoperative BG and/or HbA1c** levels be targeted for adults with diabetes undergoing elective surgical procedures?*

- 44 observational (non-RCT) studies to address this question
- majority of studies were performed in patients undergoing cardiac and orthopedic surgery
- Among the 5 studies that evaluated the effect of preoperative BG concentrations on postoperative outcomes only 2 provided data on BG concentrations on the day of surgery

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Q5.
preoperative BG and/or HbA1c target

- we suggest targeting preoperative HbA1c < 8% and BG concentrations 100 to 180 mg/dL (2⨁OOO)
- when targeting HbA1c to <8% is not feasible, we suggest targeting preoperative BG concentrations 100 to 180 mg/dL (2⨁OOO)
- Recs only for patients for whom it would be reasonable to allow time for implementation of therapies that target either a preoperative HbA1c or BG level
- BG should be within target 100 to 180 mg/dL, 1 to 4 hours prior to surgery
- Factors that may affect HbA1c levels such as anemia, hemoglobinopathies, CRF, alcoholism, drugs, and large BG variations should be taken into account

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Q 6.
Should basal or BBI vs NPH insulin be used for adults hospitalized for noncritical illness receiving ***enteral nutrition*** *with diabetes- specific and nonspecific formulations?*

- 2 systematic reviews, 1 RCT, and 3 non-RCTs that address this question
- little to no difference in mean daily BG between basal or BBI vs NPH-based regimens with cor- rectional (sliding scale) insulin.
- The panel agreed that the pharmacokinetics and pharmacodynamic profile of the insulin regimen should be matched with the mode of the enteral nutrition delivery (continuous, bolus, cyclic, etc.)

- **we suggest using NPH-based or basal bolus regimens. (2⊕OOO)**

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Q7.
Should ***noninsulin therapies*** *MET, SUs, TZDs, DPP4is, GLP-1RAs, SGLT2is vs scheduled insulin therapies be used for adults with hyperglycemia (with and without known T2D) hospitalized for noncritical illness?*

5 RCTs that compared the effects of a noninsulin agent without scheduled insulin in comparison to an insulin-only approach

No RCTs in hospitalized patients comparing insulin therapy to MET, SUs, TZDs, or SGLT2is

2 RCTs comparing GLP-1RAs with insulin therapy : small absolute reduction in risk of hypoglycemia , outweighed by a nearly 6-fold increase in nausea and/or vomiting

Several retrospective analyses identified SU use as a risk factor for hypoglycemia in the hospital

3 RCTs DPP4i : no benefit on glycemic management ; In select pts may be a reduced insulin requirement and lower frequency of hypo- glycemic events

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Q7.
*Should **noninsulin therapies** MET, SUs, TZDs, DPP4is, GLP-1RAs, SGLT2is vs scheduled insulin therapies be used for adults with hyperglycemia (with and without known T2D) hospitalized for noncritical illness?*

- In **most** adult patients with HG (w w/o known T2D) we suggest that scheduled insulin therapy be used instead of noninsulin therapies for glycemic management. (2⨁⨁OO)
  - DPP4is may be appropriate in select pts, including pts w noninsulin-requiring T2D nearing hospital discharge.
  - It may be reasonable to begin other noninsulin therapies in stable patients prior to discharge as a part of a coordinated transition plan.
- In **select** adult patients with mild hyperglycemia and T2D hospitalized for a noncritical illness, we suggest using either DPP4i with correction insulin or scheduled insulin therapy. (2⨁⨁OO)
  - Select pts: T2D w recent HbA1c < 7.5% , BG < 180 mg/dL , TDD insulin < 0.6 units/kg/day;
  - Patients who develop persistently elevated BG [eg, >180 mg/dL) on DPP4i therapy should be managed with scheduled insulin therapy;

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Q 8.
*Should **caloric CHO-containing oral fluids** vs noncaloric beverages be used preoperatively for adults with diabetes undergoing planned **elective surgical procedures?***

- In adult patients with T1D, T2D, and other forms of diabetes undergoing surgical procedures, we suggest not administering CHO-containing oral fluids preoperatively. (2⨁OOO)

ERAS: > 20 interventions : management of fluids, pain, and early mobilization

optimize perioperative nutrition with administration of CHO- beverages within a few hours before surgery

Hypothesis: insulin resistance and muscle catabolism induced by surgical stress can be dampened by preoperative oral CHO administration

Most studies, patients with diabetes excluded

1 RCT and 2 non-RCTs addressed this in patients with T2D

low to very low certainty : little to no differences in hypoglycemia, mean daily BG, and hospital LOS with or without oral caloric fluids

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Q 9.
*Should **carbohydrate counting for prandial insulin dosing** vs no carbohydrate counting (other insulin-dosing regimen) be used for adults with diabetes hospitalized for noncritical illness?*

- 1 RCT and 2 non-RCTs addressing this question
- Most patients had T2D
- mean daily BG values may be lower by 8.3 mg/dL with CC compared to fixed meal dosing
- conflicted for hypoglycemia
- most nurses trained in CC report being confident with calculating insulin doses, the opposite is true of administering doses on time
- Successful implementation of CC requires the prerequisite of nutrition and nursing education, development of menus that include information regarding the CHO content of foods, and development of protocols to guide this approach

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Q 9.
*Should **carbohydrate counting for prandial insulin dosing** vs no carbohydrate counting (other insulin-dosing regimen) be used for adults with diabetes hospitalized for noncritical illness?*

In adult patients with noninsulin-treated T2D hospitalized for noncritical illness who require prandial insulin therapy, we suggest not using CC for calculating prandial insulin doses. (2⨁OOO)

In adult patients with T1D, insulin-treated T2D hospitalized for noncritical illness, we suggest either CC or no CC with fixed prandial insulin dosing. (2⨁OOO)

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To slide or not to slide

*Q 10. Should **correctional insulin vs correctional insulin and scheduled insulin therapy (as BBI or basal insulin with correctional insulin)** be used for adults with HG (with and without known diabetes) hospitalized for noncritical illness?*

- 6 RCTs and 3 non- RCTs) to address this question
- Correction insulin used alone likely results in a 16 mg/dL (0.9 mmol/L) increase in mean daily glucose over BBI
- Correction insulin may, however, reduce the number of hypoglycemic events com- pared to BBI ± correctional insulin
- basal plus correctional insulin vs BBI therapy.
  - hypoglycemia may be lower
  - mean daily BG may be slightly higher
  - patients receiving correctional insulin alone had more frequent BG levels > 300 mg/dL and > 400 mg/dL

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Q 10. To slide or not to slide

HG (BG > 140 mg/dl), **no h/o T2D,** we suggest **initial therapy with correctional insulin** over scheduled insulin therapy (basal or basal/bolus insulin) to maintain glucose targets in the range of 100 to 180 mg/ dL .

- For persistent HG [≥2 POC-BG ≥ 180 mg/dL /24-h on correctional alone], add schedul ed insulin therapy. (2⊕OOO)

T2D, treated with **diet or noninsulin** diabetes medications prior to admission, we suggest **initial therapy with correctional insulin or scheduled insulin therapy** to maintain glucose targets in the range of 100 to 180 mg/dL .

- For persistent hyperglycemia [≥2 POC-BG ≥ 180 mg/dL / 24-h], add scheduled insulin therapy.
- Start w scheduled insulin therapy for patients w admission BG ≥ 180 mg/dL. (2⊕OOO)

T2D, insulin-treated prior to admission who are hospitalized for noncritical illness, we recommend **scheduled insulin regimen** modified for nutritional status and severity of illness to maintain glucose targets in the range of 100 to 180 mg/dL . (1⊕⊕OO)

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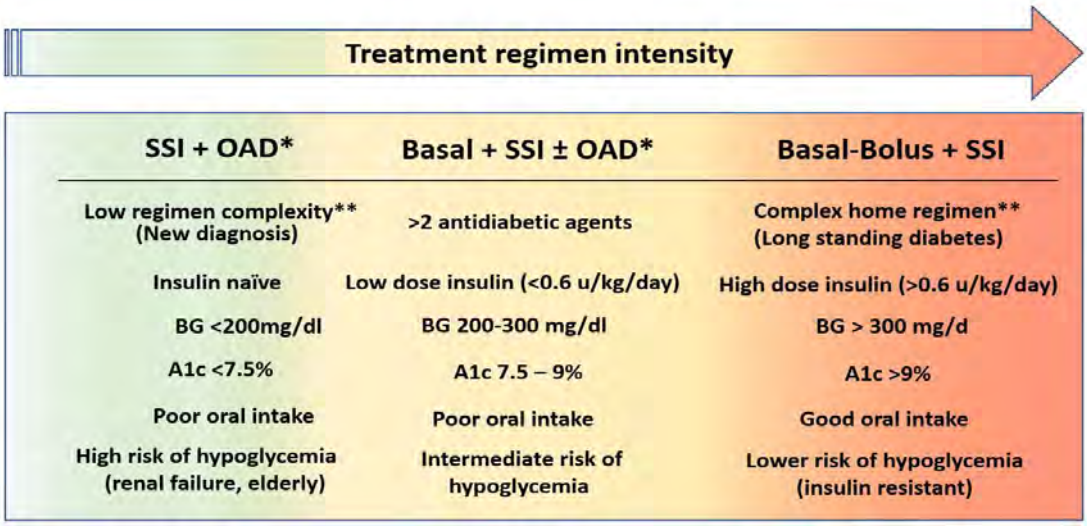
Reconsider the dogma

Individualized treatment in non-ICU patients with T2D



Pasquel & Umpierrez. Ann Intern Med 2021; **174**(8): HO2-HO4

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Key points from the guideline

- CGM can guide Rx that reduces risk for hypoglycemia
- CS/ EN are at high risk for hyperglycemia and require scheduled insulin
- Pump pts may self-manage these devices if they have the mental and physical capacity to do so with oversight
- DSME can promote improved glycemic control following discharge with reductions in the risk for hospital readmission
- Pts w DM + elective surgery may have improved postop outcomes w pre-op HbA1c ≤ 8% and BG in the immediate pre-op period < 180 mg/dL
- Pre-operative CHO beverages for pts w DM not recommended
- Pts w new HG or well-managed DM on non-insulin therapy may be treated with correctional insulin alone as initial Rx
- Scheduled insulin Rx preferred for pts w persistent BG > 180 mg/dL and recommended for pts on insulin therapy prior to admission
- DPP4 inhibitors can be used in combination with correction insulin in selected patients with type 2 diabetes who have mild HG provided there are no contraindications

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Thank you!

questions ?

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