Management of Diabetes in Advanced Chronic Kidney Disease &Hemodialysis

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KDIGO executive conclusions

Executive summary of the 2020 KDIGO Diabetes Management in CKD Guideline: evidence-based advances in monitoring and treatment

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JBDS-IP Joint British Diabetes Societies for inpatient care

Management of adults with diabetes on the haemodialysis unit

April 2016

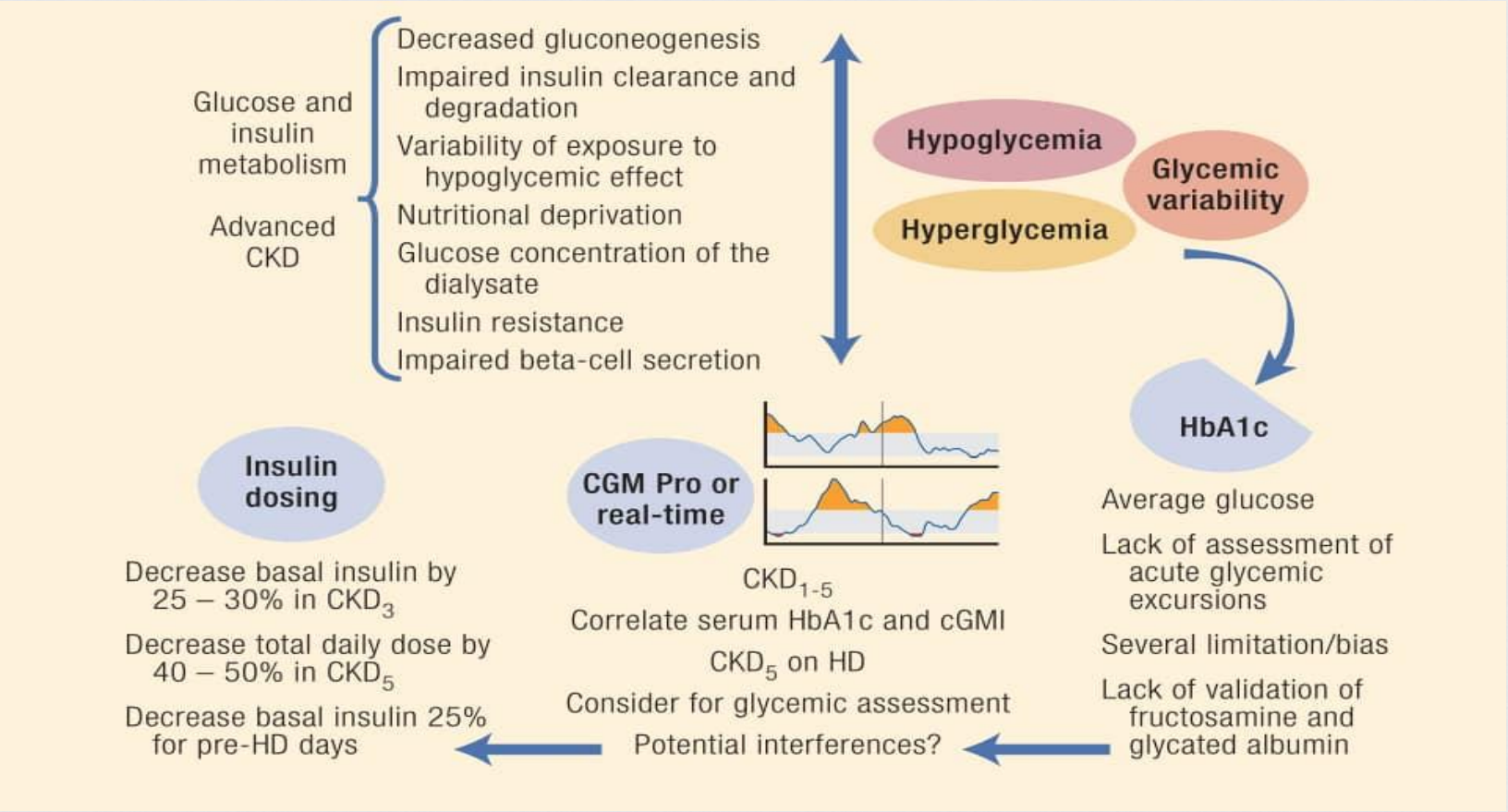
Glycemic Monitoring and Management in Advanced Chronic Kidney Disease

Rodolfo J. Galindo,[1] Roy W. Beck,[2] Maria F. Scioscia,[1] Guillermo E. Umpierrez,[1] and Katherine R. Tuttle[3,4]

Outlines

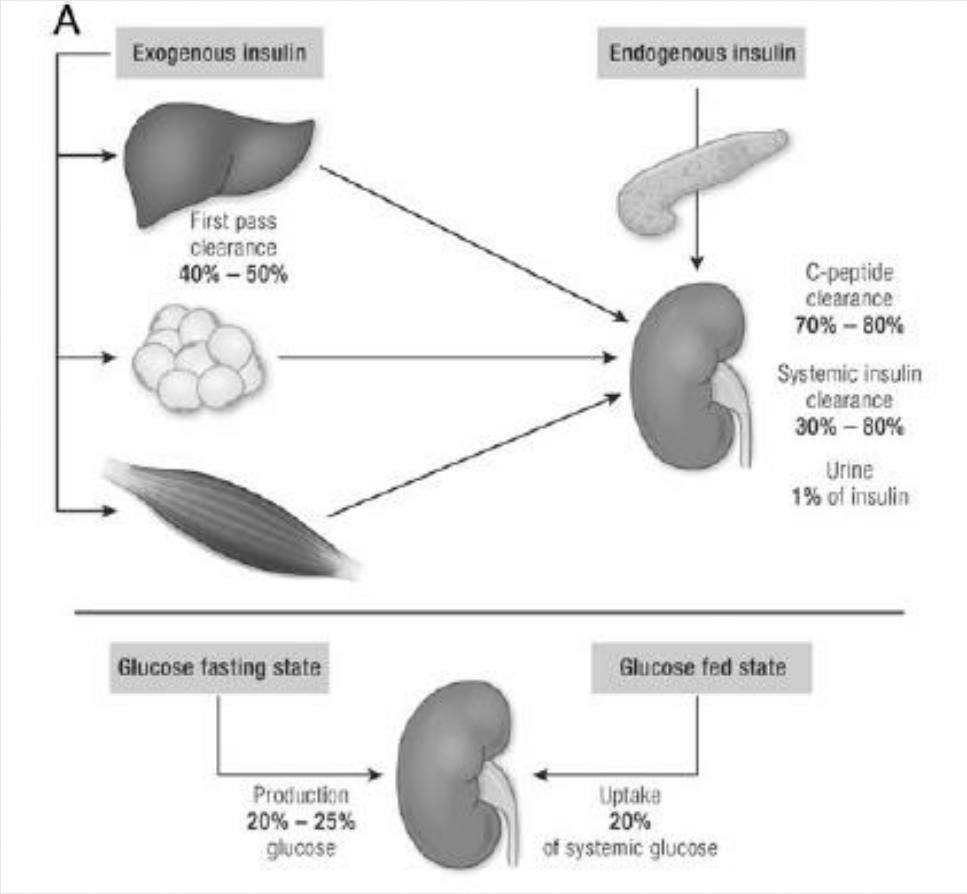
- Glucose and Insulin Metabolism
- Glycemic monitoring and targets in CKD/haemodialysis
- Limitations of glycemic biomarkers
- Self-monitoring of blood glucose
- CGM in CKD & Hemodialysis
- Anti hyperglycemic therapies
- Management Of Hyperglycemia In Hospital/ Dialysis Unit
- Management Of Hypoglycemia In Hospital/ Dialysis Unit

Glucose and Insulin Metabolism



Galindo et al Glycemic Monitoring and Management in Advanced CKD Endocrine Reviews, October 2020

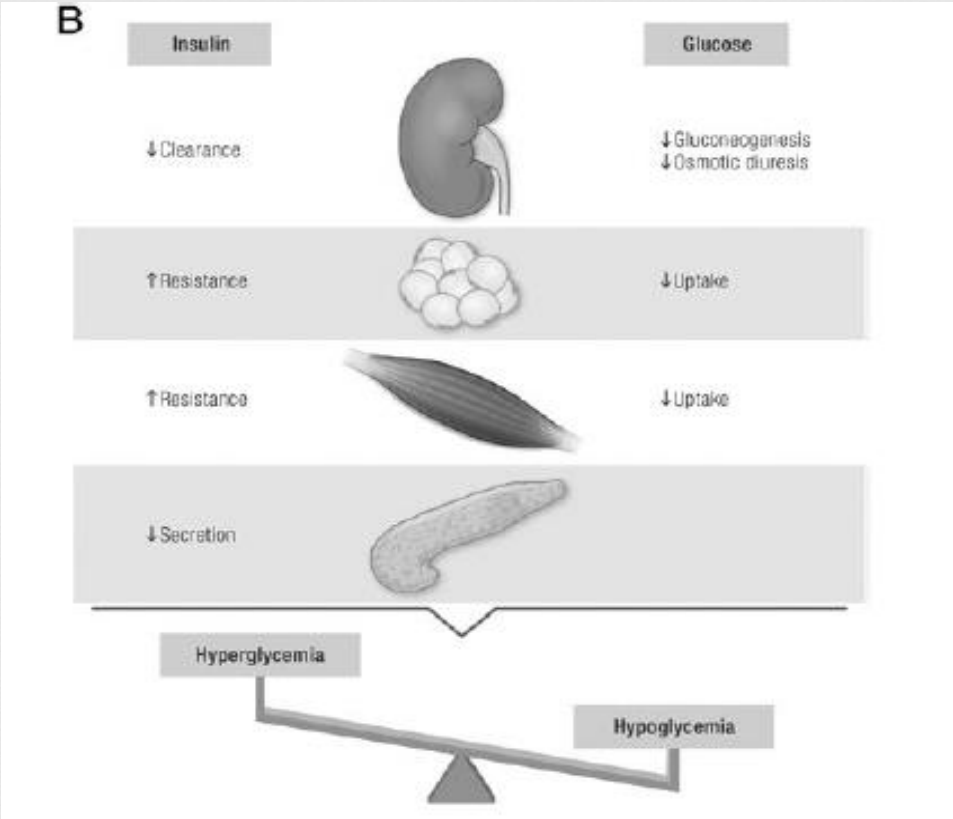
Glucose and Insulin Metabolism



Insulin and glucose metabolism with normal renal function

Galindo et al Glycemic Monitoring and Management in Advanced CKD Endocrine Reviews, October 2020

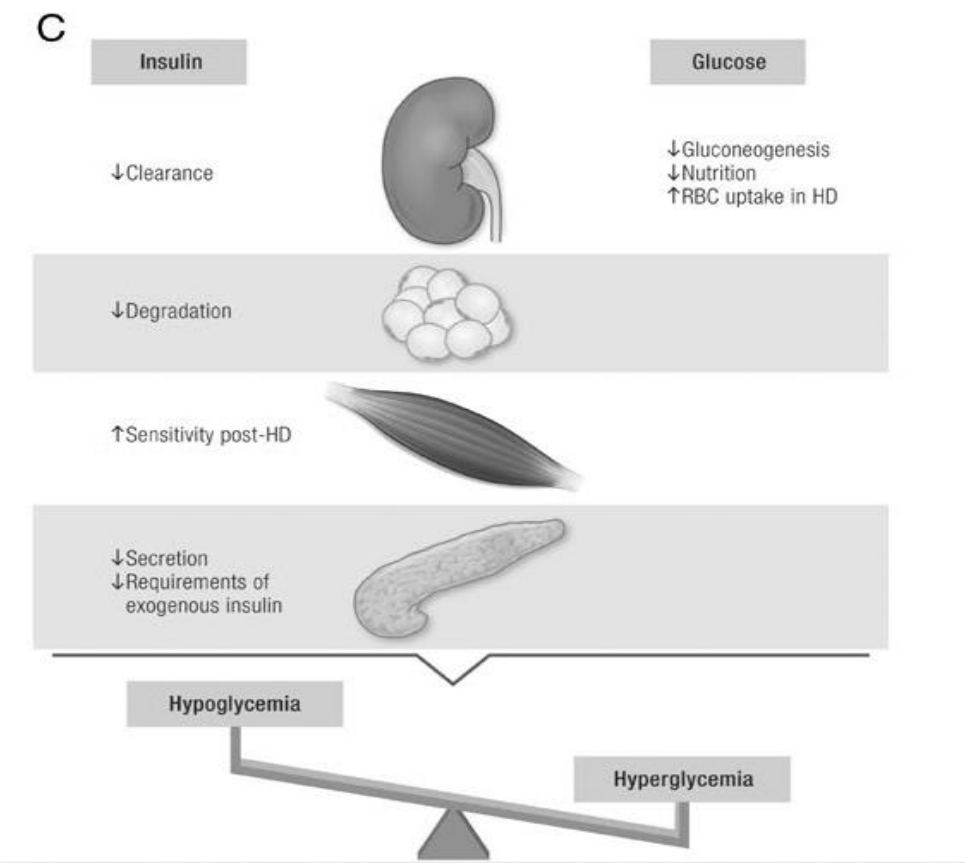
Glucose and Insulin Metabolism



Insulin and glucose metabolism in early chronic kidney disease

Galindo et al Glycemic Monitoring and Management in Advanced CKD Endocrine Reviews, October 2020

Glucose and Insulin Metabolism



Insulin and glucose metabolism in advanced chronic kidney disease &hemodialysis

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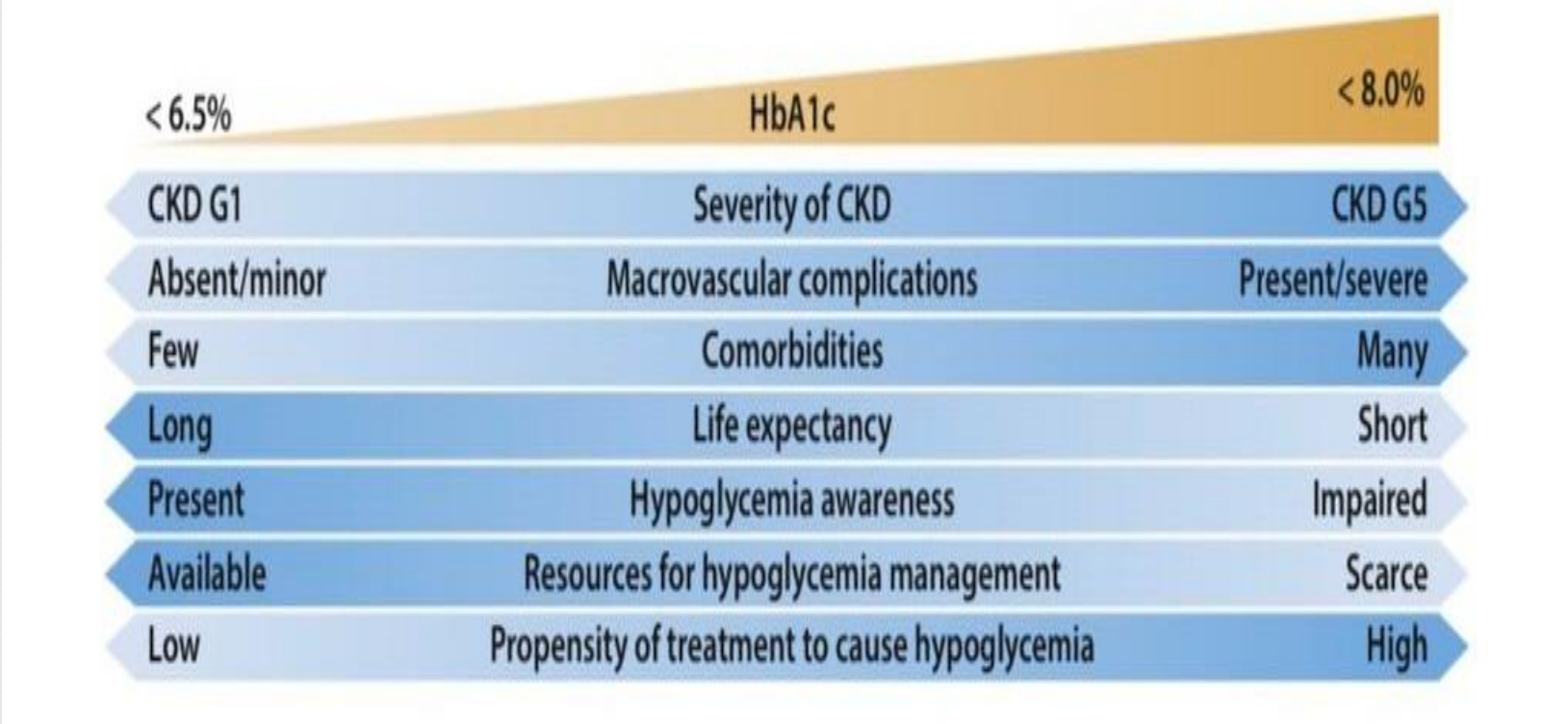
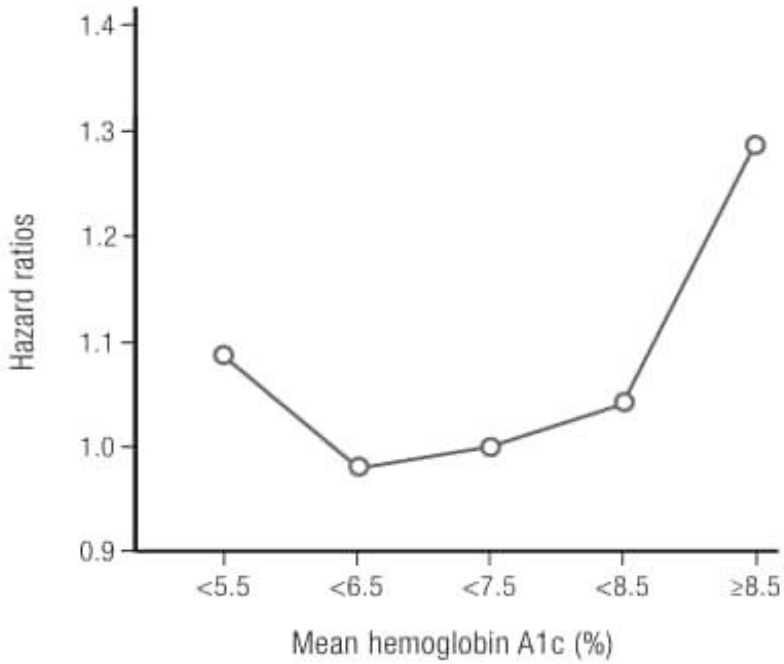
Glycemic monitoring and targets in CKD



Factors guiding decisions on individual glycated hemoglobin (HbA1c) targets

IH de Boer et al.: KDIGO guideline on diabetes in CKD (2020)

Glycemic monitoring and targets in hemodialysis



Association of mean hemoglobin A1c and adjusted all-cause mortality risk in patients with diabetes on hemodialysis: results of a meta-analysis of 10 studies (n = 83 684 patients).

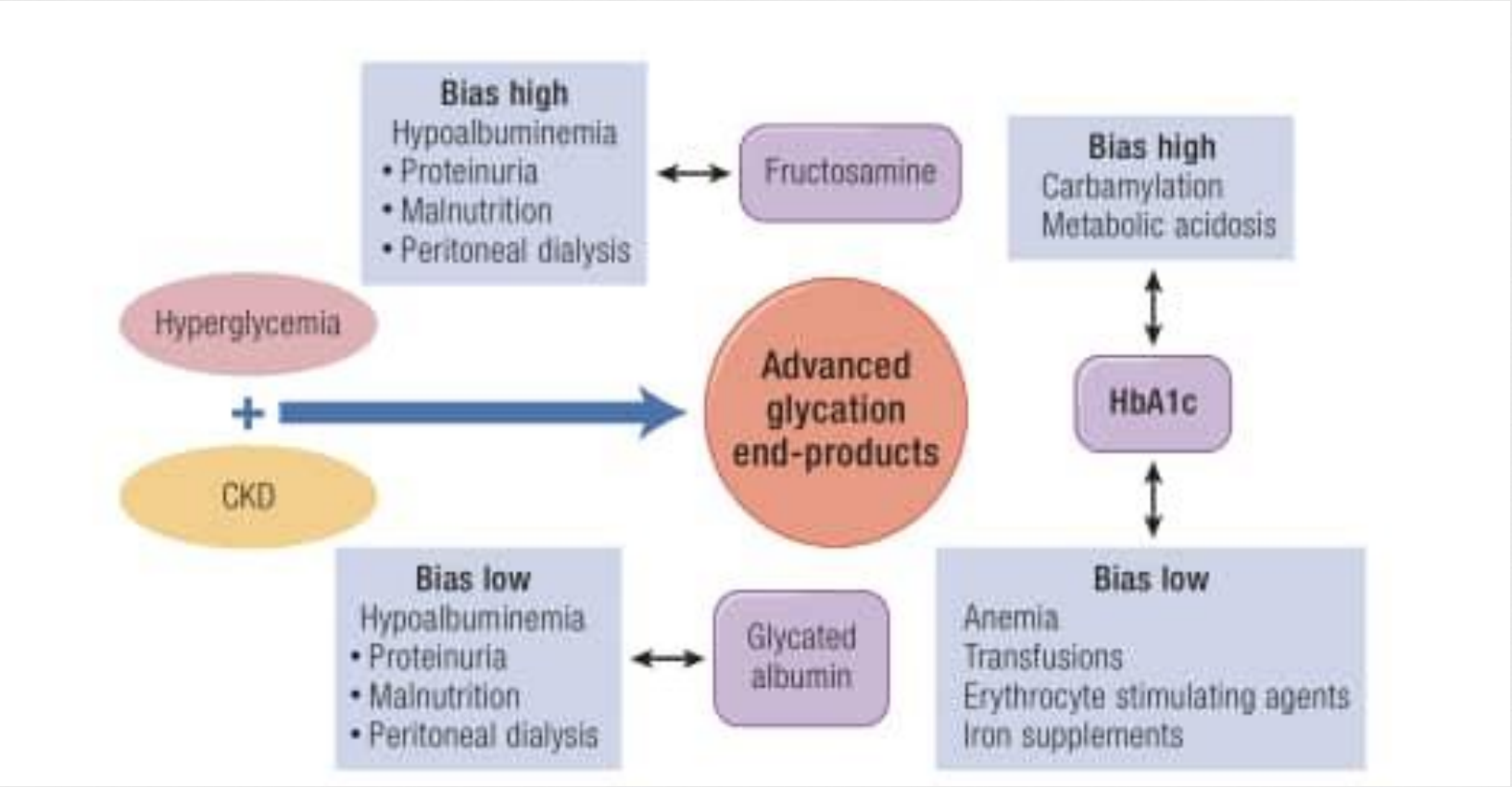
Galindo et al Glycemic Monitoring and Management in Advanced CKD Endocrine Reviews, October 2020

Glycemic monitoring and targets in hemodialysis

- The target for HbA1c should be individualized but if the patient is on a hypoglycemia inducing treatment should be aimed (7.5–8.5%)
- It is likely that HbA1c (9.5%) represents poor glycemic control unless there is severe iron deficiency
- Reduction in treatment should be considered for patients with HbA1c< (7.5%) on treatments associated with increased risk of hypoglycemia

Management of adults with diabetes on the haemodialysis unit *British Journal of Diabetes* 16.2 (2016): 69-77

Limitations of glycemic biomarkers



Galindo et al Glycemic Monitoring and Management in Advanced CKD Endocrine Reviews, October 2020

Limitations of glycemic biomarkers on hemodialysis

- Potential for overestimation of HbA1c in ESRD

- An increased level of blood urea nitrogen
- Uremia
- Iron deficiency
- Metabolic acidosis

Management of adults with diabetes on the haemodialysis unit *British Journal of Diabetes* 16.2 (2016): 69-77

Limitations of glycemic biomarkers on hemodialysis

- Potential for underestimation of HbA1c in ESRD

- Shortened erythrocyte lifespan
- Blood transfusions
- The widespread use of erythropoietin

- Despite the above, HbA1c is still recommended in current guidelines as the main biomarker for assessing glycaemic control in people with CKD

Management of adults with diabetes on the haemodialysis unit *British Journal of Diabetes* 16.2 (2016): 69-77

Limitations of glycemic biomarkers on hemodialysis

- Alternative markers of glycemic control

- fructosamine and glycated albumin (GA) have been proposed as potentially better surrogate markers of glycemic control in patients with renal anemia and in receipt of erythropoietin

- The concentration of fructosamine is influenced strongly by serum protein concentrations and by low molecular weight substances such as urea or uric acid

Management of adults with diabetes on the haemodialysis unit *British Journal of Diabetes* 16.2 (2016): 69-77

Limitations of glycemic biomarkers on hemodialysis

- Glycated albumin may offer the opportunity to assess glycaemic control over a shorter time period (15–20 days) and with greater accuracy in patients with diabetes on maintenance haemodialysis

Management of adults with diabetes on the haemodialysis unit *British Journal of Diabetes* 16.2 (2016): 69-77

Self-monitoring of blood glucose

- SMBG is especially important in subjects receiving treatments that may cause hypoglycemia, those who suffer from regular hypoglycemia and those with hypoglycemia unawareness

- In patients on MHDx SMBG results can also be affected by hemolysis, anticoagulation, hyperlipidemia and metabolic acidosis

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Self-monitoring of blood glucose

- Methods for glucose measurement

1) glucose oxidase-based (GO)
2) hexokinase-based (HK)
3) glucose dehydrogenase-based (GDH)

Self-monitoring of blood glucose

- high levels of acetaminophen, ascorbic acid, icodextrin, maltose, triglycerides, uric acid, or abatacept react with the sensor's electrode or have cross-reactivity with the enzyme

- low hematocrit (< 35%) may result in falsely high glucoses in the glucose meter using the GO technique

- high acetaminophen plasma levels (> 8 mg/dl) may result in falsely high blood glucose readings

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Self-monitoring of blood glucose

- Hypoxia (partial pressure of oxygen < 45 mmHg) or oxygen therapy (partial pressure of oxygen > 150 mmHg) may cause falsely high and low glucose in GO-based meters, respectively

- High levels of triglycerides, uric acid (> 20 mg/dL), or bilirubin may cause pseudo hypoglycemia

CGM in CKD & Hemodialysis

- **CGM** providers to recognize glucose patterns, including responses glucose patterns, including responses to meals, medications, acute illness, or other stressors

- **CGM** use has the advantage of providing better assessment of glycemic patterns and insulin needs

- **CGM** has the potential to become a new standard of care for assessment of glycemic control in diabetic patients treated by maintenance hemodialysis

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Glycemic monitoring

Population	HbA1c	Frequency	Glycemic indexing by CGMI	Insulin requirements
CKD stages 1 to 5	Yes	Twice per year Up to 4 times per year if not achieving target or change	Correlate interstitial glucose with HbA1c for individual patients	Lower 25% to 30% basal insulin dose for patients with T1D and CKD3
CKD stage 5 on dialysis	No	Not applicable	consider	-Lower 50% TDD for T2Dpatients with CKD5 -Lower total daily insulin dose by 35%to 40% for patientT1Dwith CKD 5 - Lower (25%) basal insulin dose for pre HD

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Antihyperglycemic therapies

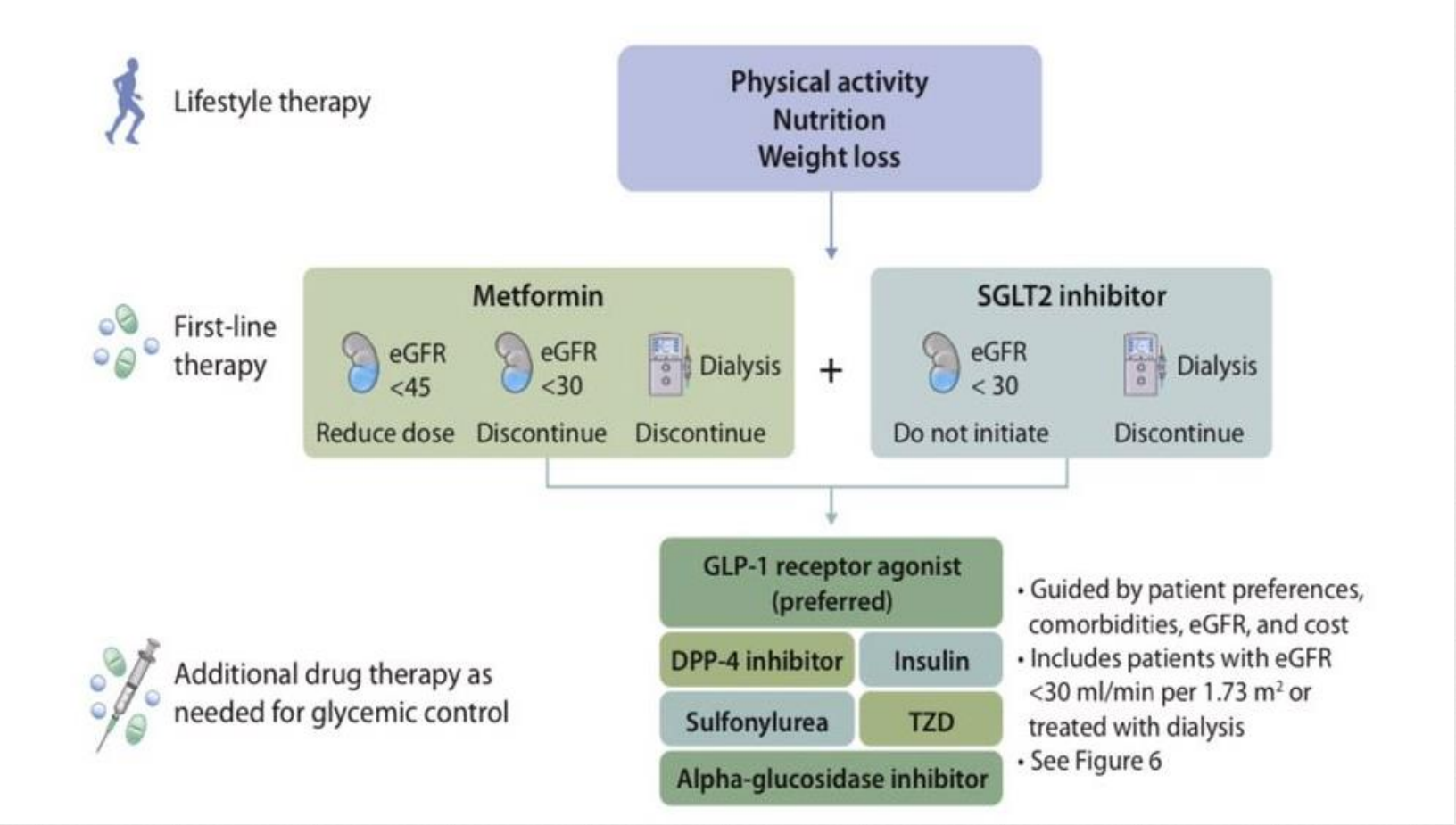
Drug	Trial	Kidney-related eligibility criteria	Primary outcome	Effect on albuminuria	Effect on GFR loss	Adverse effects
Empagliflozin	EMPA-REG OUTCOME	GFR ≥30 ml/min	MACE↓	↓↓	↓↓	Genital mycotic infections, DKA
Liraglutide	LEADER	GFR ≥15 ml/min	MACE↓	↓	↔	GI
Exenatide	EXSCEL	GFR ≥30 ml/min	MACE↔	↔	↔	None notable
Sitagliptin	SAVOR-TIMI 53	GFR ≥30 ml/min	MACE↔	NA	NA	None notable
Linagliptin	CARMELINA	GFR ≥15 ml/min	Progression of ↔CKD	↓	↔	None notable

placebo-controlled clinical outcome trials assessing the benefits and harms of (SGLT2) inhibitors, (GLP-1) receptor agonists, and (DPP-4) inhibitors

MACE, major adverse cardiovascular events including myocardial infarction, stroke, and cardiovascular death

IH de Boer et al.: KDIGO guideline on diabetes in CKD (2020)

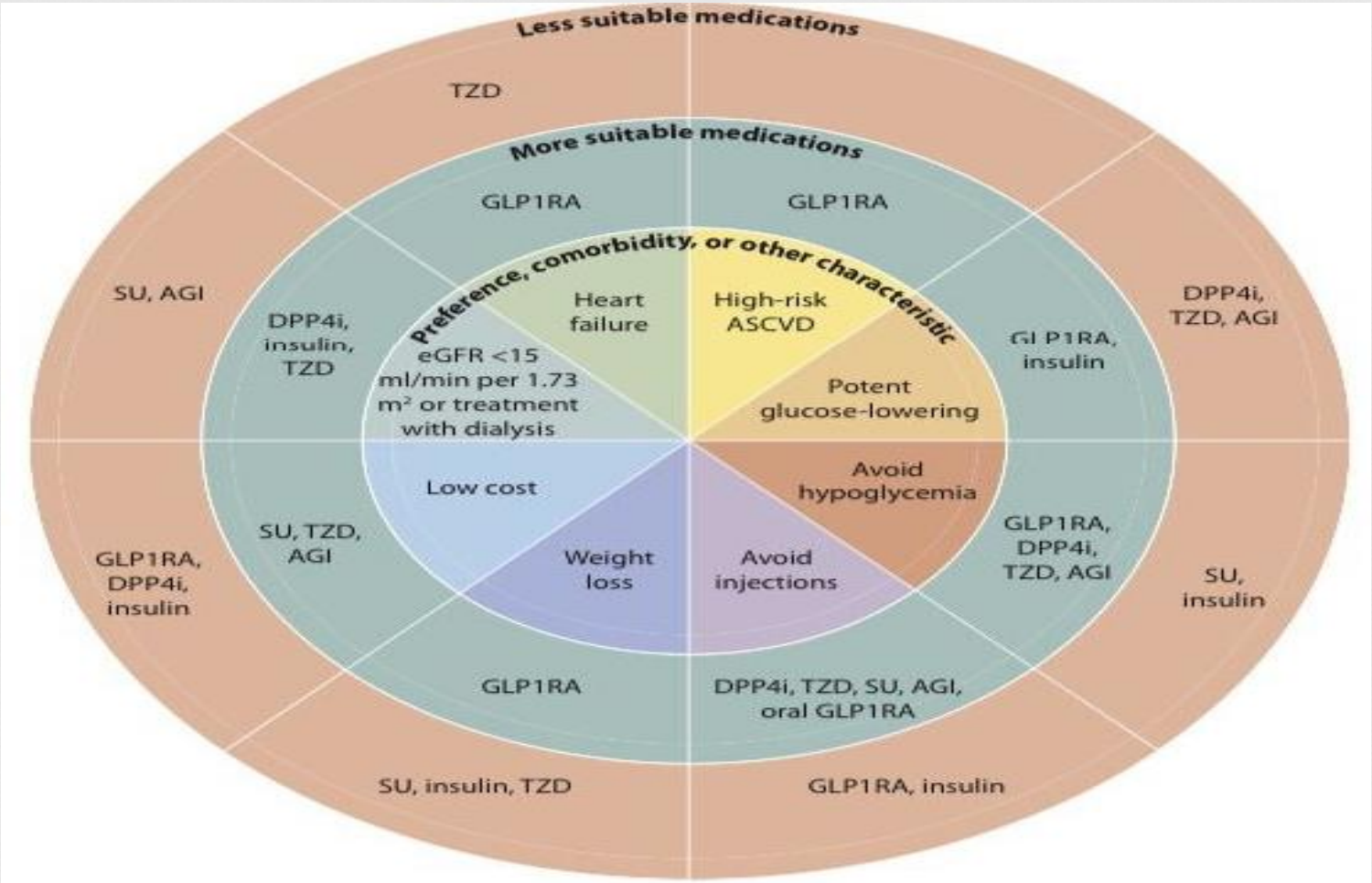
Antihyperglycemic therapies



Treatment algorithm for selecting antihyperglycemic drugs for patients with type 2 diabetes and chronic kidney disease

IH de Boer et al.: KDIGO guideline on diabetes in CKD (2020)

Antihyperglycemic therapies



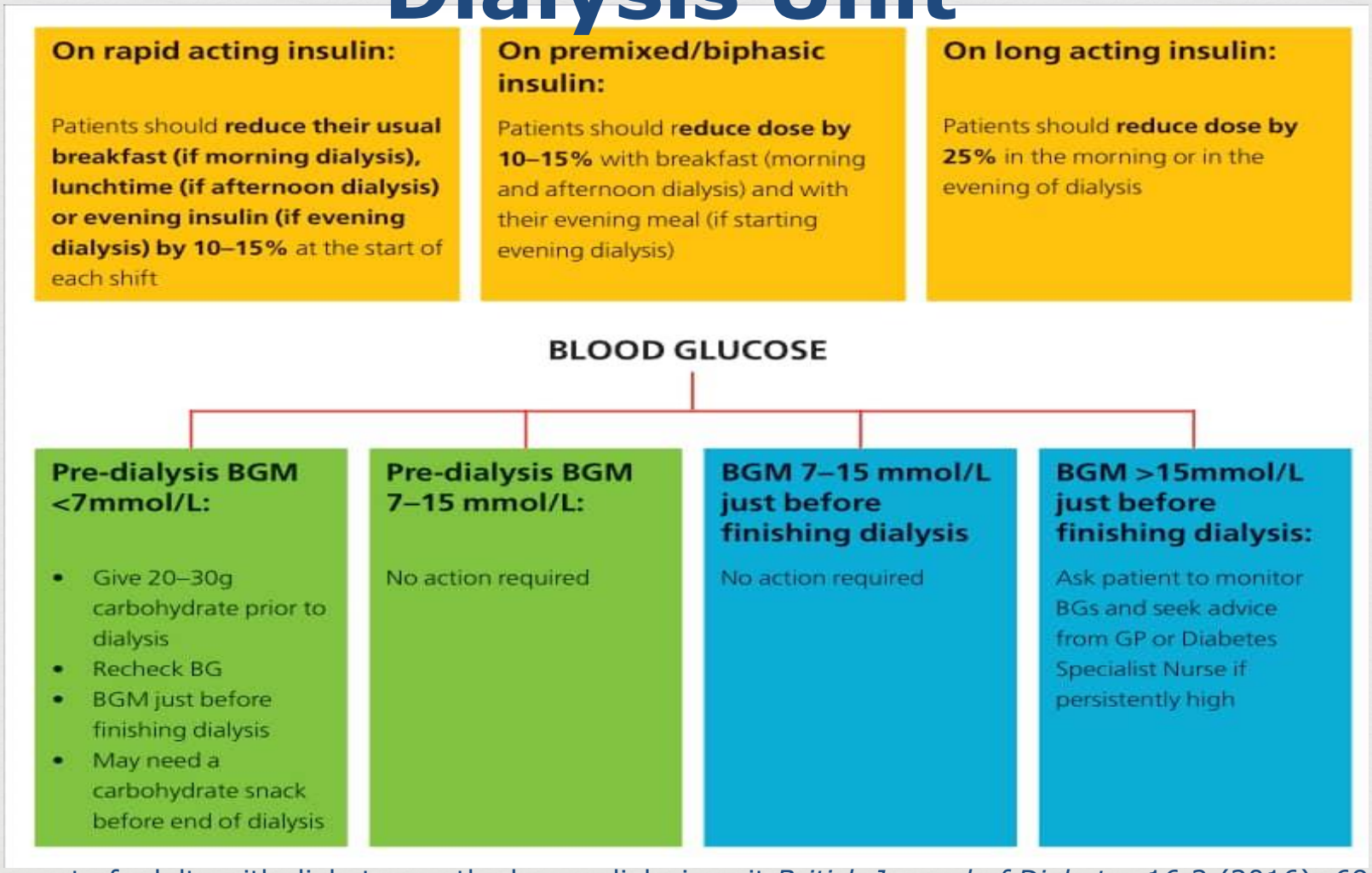
Patient factors influencing the selection of glucose-lowering drugs

IH de Boer et al.: KDIGO guideline on diabetes in CKD (2020)

Medication	Metabolism	Labeling dosing by GFR	Dose in ESKD and/or dialysis
Metformin	Kidney	-No dose adjustment if eGFR > 45 mL/min -Do not start and reduce dose if already on therapy and eGFR 30 to 45 mL/min -Discontinue if eGFR < 30 mL/min/	Contraindicated because of risk of lactic acidosis
Glipizide	Liver Excretion of < 10% of unchanged drug in urine	No dose adjustment if eGFR > 50 mL/min	No adjustment, but conservative initial dose (2.5 mg daily) recommended Use with caution
Glimepiride	Liver Excretion in urine 60% of drug	Consider alternative if eGFR < 15 mL/min/1.73 m2	Start lower dose of glimepiride (eg, 1 mg daily), caution recommended because of risk of hypoglycemia
Glyburide	Kidney Excretion of 50% of drug in urine	Avoid use	Contraindicated
Repaglinide	Liver Minimal excretion of parent drug in urine	No dose adjustment if eGFR > 30 mL/min/1.73 m2	Initiate conservatively at 0.5 mg with meals if eGFR < 30 mL/min/1.73 m2
Sitagliptin	Kidney Excretion of 87% of unchanged drug in urine	100 mg daily if eGFR > 50 mL/min/1.73 m2 50 mg daily if eGFR 30 to 50 mL/min/1.73 m2 25 mg daily if eGFR < 30 mL/min/1.73 m2	Maximum dose of 25 mg daily
Linagliptin	Liver Excretion of < 5% to 7% of drug in urine	No dose adjustment	No dose adjustment

Medication	Metabolism	Labeling dosing by GFR	Dose in ESKD and/or dialysis
Exenatide	Proteolytic degradation following glomerular filtration Excretion of majority of dose in the urine	No dose adjustment if eGFR > 50 mL/min/1.73 m2 Caution when initiating or escalating doses if eGFR 30 to 50 mL/min/1.73 m2 Not recommended with eGFR < 30 mL/min/1.73 m2	Contraindicated
Liraglutide	Proteolytic degradation (not specific organ as a major route of elimination) Intact drug not detected in urine	No dose adjustment Post-marketing studies showed increased risk of gastrointestinal effects with higher doses Monitor for gastrointestinal reactions in patients with CKD	No dose adjustment Postmarketing studies showed increased risk of gastrointestinal effects with higher doses
Empagliflozin	Liver Excretion of25% to 50% of unchanged drug in urine	No dose adjustment required if eGFR ≥ 45 mL/min/1.73 m2	Avoid use and discontinue in patients with eGFR persistently < 45 mL/min/1.73 m2
Acarbose	Intestinal	Avoid if eGFR < 30 mL/min/1.73 m2	Contraindicated
Pioglitazone	Liver Excretion of negligible amount of unchanged drug in urine	No dose adjustment	No dose adjustment recommended Caution with use given fluid retention and adverse effects on bone metabolism

Management Of Hyperglycemia In Hospital/ Dialysis Unit



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Management Of Hypoglycemia In Hospital/ Dialysis Unit

Hypoglycaemia is blood glucose <4 mmol/L and may be asymptomatic

(If pre-dialysis blood glucose < 7 mmol/L, give 20–30g carbohydrate prior to dialysis)

Mild hypoglycaemia	Moderate hypoglycaemia	Severe hypoglycaemia
Sweaty	Tingling lips/fingers	Decreased consciousness
Shaky	Visual disturbance	Fitting
Pale/hungry	Anxious/restless (confusion)	Coma

HYPOGLYCAEMIA

If conscious, give:

- **3–4 Dextrose tablets (5 g/tablet) or**
- **1½ Glucogel (10 g/tube) or**
- **1 cup Lucozade (90–120 mL) or 4 Jelly Babies/ 8 Jelly Beans (20g)**

If symptoms improve after 15 minutes and BGM >4 mmol/L, give 10–20g complex carbohydrate (biscuit, milk, toast or sandwich) and recheck blood glucose to ensure response

If symptoms do not improve after 15 minutes, repeat above treatment. If BGM still <4 mmol/L, call the Medical Team immediately

If unconscious, call the Medical Team:

Simultaneously also give:

- **20% Dextrose 100 mL** over 15 minutes
- **1 mg glucagon injection** (i.m. or s.c. if no i.v. access)

Once conscious, give 10–20 complex carbohydrate (biscuit, milk, toast or sandwich) and recheck blood glucose in 15 minutes

Ask the Medical Team to review medications/insulin before discharge

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