A practical approach to managing diabetes in the perioperative period

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Diabetes mellitus (DM) is a common multisystem disease with hyperglycaemia as the hallmark. It is a modifiable risk factor of complications after surgery. The incidence of DM and its impact on public health are steadily increasing globally. In South Africa (SA), it is estimated that a large proportion of people living with DM are undiagnosed. A number of international groups have addressed the problem of DM in the perioperative period, proposing guidelines for optimisation and management of these patients. The guidelines fail to address the variety of contexts within which surgery is delivered in SA. In this review, the authors discuss DM within the SA context. The article provides a range of approaches to managing the patient with DM in the perioperative period. Importantly, the perioperative healthcare provider's approach should be steered by a local multidisciplinary team that considers the evidence base in light of their resource and patient context.

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The burden of non-communicable disease in South Africa (SA) is escalating. Undiagnosed and uncontrolled diabetes mellitus (DM) are common in patients requiring surgery. Access to resources and expertise to safely control blood glucose levels in the perioperative period are variable in the SA public healthcare system. The combination of an increasing burden of disease and inadequate perioperative diabetes management is likely to increase surgical complication rates, mortality and cost of care.

This article focuses on perioperative diabetes management of type 1 and type 2 DM patients who are undergoing surgery in a non-critical care setting. Obstetric, paediatric and critical care patients are excluded from this discussion.

Burden of disease

Type 2 DM is the most common type of diabetes, representing >90% of the DM disease burden in SA. The International Diabetes Federation reports that there are currently ~1.8 million adults in SA known to have DM, while a further 1.5 million adults remain undiagnosed.[1] The SA National Health and Nutrition Examination Survey (SANHANES) 2012 showed a national prevalence of abnormal glucose regulation of 18.6%, varying according to ethnicity and degree of urbanisation. According to SANHANES, 45% of people with diabetes were previously undiagnosed.[2]

Over the past decade, DM has become one of the major underlying causes of mortality globally; in SA it now ranks second only to tuberculosis.[3]

The SA Surgical Outcomes Study (SASOS) reports a 10.2% prevalence of diabetes in our surgical population (5.8% non-insulin dependent, and 4.4% insulin dependent).[4]

Diabetes mellitus in the perioperative context

The perioperative period is associated with worsening glycaemic control, probably due to the stress response of surgery.[5] Starvation, tissue trauma and pain lead to increased levels of pro-inflammatory mediators and circulating stress hormones. These substances alter insulin secretion and sensitivity, producing a state of relative insulin resistance, protein catabolism and lipolysis with liberation of free fatty acids. This state can extend for multiple days into the postoperative period, driving adverse patient outcomes.[6] These include increased mortality, increased length of hospital stay, as well as increased infective (surgical site infections, urinary tract infections and pneumonia) and non-infective complications (cardiac events, acute kidney injury and stroke).[7]

Protocol-driven quality improvement projects result in improved perioperative glycaemic control, but strict control strategies increase hypoglycaemic events.[8,9] As hypoglycaemia has been linked to mortality, it is essential to avoid the condition by targeting a perioperative blood glucose level in the range of 6.0 - 10.0 mmol/L.[10] A capillary blood glucose (CBG) measurement up to 12.0 mmol/L may be tolerated for brief periods if it is regularly monitored and expected to decrease.[11,12]

Hyperglycaemia in the perioperative period may be due to physiological stress and should not be diagnosed as DM without input from the local diabetes healthcare provider. Stress hyperglycaemia without DM is a poorly understood entity, the management of which remains unclear.[5]

Perioperative management

Consider perioperative management of DM in three phases: preoperative, intraoperative, and postoperative.

Preoperative

In the preoperative phase the patient with DM must be identified and assessed to define a perioperative management plan. Screen for undiagnosed DM according to the Society for Endocrinology, Diabetes and Metabolism of SA (SEMDSA) guidelines.[13] Evaluate the diabetic patient's capacity to manage the disease, chronic glycaemic

control and invasiveness of the planned surgery. Where available, a glycated haemoglobin (HbA1c) should be used to determine adequacy of glycaemic control in those diagnosed with diabetes. An elevated HbA1c correlates with poor patient outcomes after surgery and an HbA1c >8.5% (69 mmol/mol) warrants postponement of elective surgery.[11,12] More stringent cut-off values are recommended by some, but may currently be unattainable in many parts of SA.[14]

The patient's comorbidities and glycaemic control should always be optimised before elective surgery. In an emergency, there is little time for optimisation, as surgery must proceed promptly. Often though, patients present for surgery that is time sensitive. In this 'grey zone' between elective and emergency, the timing of surgery should be determined by a multidisciplinary team with a patient-centred discussion about how best to balance risk and benefit.[15] The decision to proceed with surgery in the face of uncontrolled DM must acknowledge the increased risk to the patient and define ways to manage this risk.

Resources and access to expertise vary among healthcare centres. It is therefore important to choose an appropriate perioperative glycaemic management plan. Although many options are available, four are commonly used and recommended (Table 1):

- modification of usual treatment (Tables 2 and 3)
- basal-bolus subcutaneous (SC) insulin (Fig. 1)
- Alberti's glucose-insulin-potassium (GIK) intravenous infusion (Box 1)
- variable rate intravenous insulin infusion (VRIII) (Fig. 2).

Monotherapy with SC short- or rapid-acting insulin according to a sliding scale is *not* recommended for in-hospital management of DM, as it increases the risk of hypoglycaemia and provides inferior glycaemic control.[16,17]

In all cases, limiting of the starvation period has to be planned, as well as where the patient will be managed postoperatively (day case, surgical ward or high-care facility). For short starvation periods (one missed meal), modification of the usual medication will often suffice (Tables 2 and 3). Missing more than one perioperative meal is considered a prolonged starvation period. If the CBG is >12 mmol/L, it will necessitate either basal SC insulin or an intravenous insulin infusion.

Intraoperative

The intraoperative phase starts at the time of arrival in theatre and continues until transfer to the postoperative ward. The patient with DM must have a documented CBG prior to commencement of anaesthesia. While under anaesthesia, the CBG should be monitored at least 2-hourly, more frequently if abnormal and in patients receiving insulin.[18] If the intraoperative CBG levels were abnormal, the CBG measurement should be repeated in the post-anaesthetic recovery area.

When possible, administer SC short- or rapid-acting insulin to avoid unnecessary intravenous insulin for short surgical procedures. Limit SC short- or rapid-acting insulin to two intraoperative doses. In type 2 DM, a first dose of 0.1 U/kg (up to a maximum of 6 U) is appropriate; alternatively, use the correction dosing scale in Fig. 1 as a starting point. To prevent insulin stacking intraoperatively, do not administer a top-up dose of SC insulin within 2 hours of the first dose. Intravenous insulin is preferred when SC insulin does not control hyperglycaemia. This is common in surgery of longer duration, prolonged starvation and emergency cases.[11]

Table 1. Indications, advantages and disadvantages of four perioperative diabetes management strategies

Management	Indications	Advantages	Disadvantages
Modification of usual therapy	HbA1c <8.5% Short starvation period (<1 meal missed)	Lowest risk for hypoglycaemia Decreased burden on ward staff Suitable for patient self-management	Often not possible, as patients have poor baseline control or there is prolonged starvation
Basal-bolus SC insulin with correction doses	Those already on basal-bolus insulin Type 1 diabetes Patients with poor baseline control Newly diagnosed DM requiring perioperative insulin therapy Short surgical duration Where IV insulin therapy is not feasible	Improved glycaemic control Flexible dosing Decreased risk of hypoglycaemia	Intensive Regular monitoring required Not to be used if the patient is not eating meals Unpredictable absorption when there is impaired tissue perfusion
Alberti's glucose-insulin-potassium infusion	Poor control on SC insulin (CBG >12.0 mmol/L) Prolonged starvation period (>1 meal missed) Long surgical duration Periods of inadequate tissue perfusion High-care or ICU setting VRIII is not an option	Improved glycaemic control Flexible	Labour intensive Need trained staff Risk of hypo-Na^+/K^+ Risk of hypoglycaemia
VRII	Poor control with SC insulin (CBG >12.0 mmol/L) Prolonged starvation period (>1 meal missed) Long surgical duration Periods of inadequate tissue perfusion High-care or ICU setting	Improved glycaemic control Flexible	Requires specialised equipment Labour intensive Need trained staff Risk of hypo-Na^+/K^+ Risk of hypoglycaemia

SC = subcutaneous; DM = diabetes mellitus; IV = intravenous; CBG = capillary blood glucose; ICU = intensive care unit; VRIII = variable rate intravenous insulin infusion.

Table 2. Summary of non-insulin antidiabetic agents with recommendations for perioperative management[21,22]

Management	Class of drug (examples)	Considerations	Recommendations
Insulin sensitisers	Biguanides Metformin	Does not cause hypoglycaemia Risk of lactic acidosis	Continue while eating Omit on day of surgery Omit if risk of renal impairment (IV contrast, other nephrotoxic agents, haemodynamic instability) Omit if >1 meal missed
	Thiazolidinediones Pioglitazone (roziglitazone)	Does not cause hypoglycaemia Concern of hepatotoxicity Contraindicated in haemodynamic instability	Omit on day of surgery Restart when tolerating meals
Secretagogues	Sulphonylureas Glibenclamide Gliclazide Glimepiride	Risk of hypoglycaemia	Omit while fasting Restart when tolerating meals
	Meglitinides Repaglinide Nateglinide	Risk of hypoglycaemia	Omit while fasting Restart when tolerating meals
Incretin family	GLP-1 analogues Exenatide Liraglutide	Delayed gastric emptying concern for aspiration risk Injectable only	Limited information May improve perioperative glycaemic control
	DPP-4 inhibitors (gliptins) Saxagliptin Vildagliptin		Limited information May improve perioperative glycaemic control
Increased glucosuria	SGLT-2 inhibitors (gliflozins) Empagliflozin Dapagliflozin	Association with DKA	Avoid in the perioperative period
Impairs absorption	Alpha-glucosidase inhibitors Acarbose	Causes severe flatulence and bloating	Avoid in the perioperative period

GLP-1 = glucagon-like peptide 1; DPP-4 = dipeptidyl peptidase-4; SGLT-2 = sodium-glucose co-transporter 2; DKA = diabetic ketoacidosis; IV = intravenous.

Table 3. Perioperative modification of insulin therapy*†

Insulin regimen‡	Day before surgery	Day of surgery
Once daily (evening dosing) intermediate- or long-acting insulin	Reduce dose by 20%	Restart insulin with evening meal
Once daily (morning dosing) intermediate- or long-acting insulin	Usual dose	Reduce dose by 20%
Twice daily dosing	Usual dose	Reduce morning dose to 50%
Premixed insulin, or intermediate- or long-acting insulin		Normal evening dose with dinner
Basal-bolus regimen	Usual bolus doses Reduce night-time basal dose by 20%	If basal dose in the morning, reduce by 20% Omit bolus doses while fasting

*Adapted from the Joint British Diabetes Society for Inpatient Care guidelines, with permission.[11]
†Appropriate where no more than one meal missed in the perioperative period.
‡Check capillary blood glucose regularly while fasting. The majority of international guidelines advise 1- or 2-hourly measurements. Protocols with a 4-hourly measurement interval carry a 10% hypoglycaemia risk.[18]

Postoperative

After surgery, intravenous insulin therapy must not be discontinued without overlapping and restarting the patient's basal SC insulin. Check the CBG before discharge from the post-anaesthetic recovery area. Ensure that the patient is sent to the appropriate level of care for continuation of their glycaemic control strategy. Early reinstatement of normal enteral feeding and usual antidiabetic medication is the goal. The agents and regimen used for glycaemic control will largely depend on the feeding status of the patient (Table 4).

Safe insulin therapy

Insulin is an extremely potent agent. Drug errors can cause significant harm to the patient. Staff education and involvement of the local pharmacy are needed to ensure constant safe prescribing, dispensing and dosing practices.[19]

There is a real risk of diabetic ketoacidosis (DKA) with transition to and from intravenous insulin therapy. Delays in commencing the intravenous insulin infusion, and discontinuation of the infusion prior to administration of basal insulin, cause acute insulin deficiency in insulin-dependent patients.[20] This risk can be mitigated by continuation of basal SC insulin while using intravenous insulin, or by administration of intermediate- or long-acting insulin 30 minutes before discontinuing the intravenous insulin (GIK or VRIII).[12]

Non-insulin antidiabetic agents

Non-insulin antidiabetic agents should not be started in the immediate perioperative period. These medications have multiple contraindications and are not rapidly titratable. However, diabetic patients who are well controlled could be considered for continuation of their non-insulin agents during the perioperative period. Guidance

Three components
- Basal – once daily intermediate- or long-acting insulin
- Bolus – dosing at meal times with short- or rapid-acting insulin
- Correction – additional dosing at meal times with short- or rapid-acting insulin to achieve or maintain the desired individualised glycaemic target

For patients already on insulin, start with the patient's usual TDD

For insulin-naive patients, start with a TDD of 0.2 - 0.3 U/kg/day

↓

Give 50% of the TDD as basal insulin
Give 50% of the TDD as bolus doses (divide into 3 equal doses and give before each meal)

↓

Give correction doses (added to the already prescribed insulin doses) according to the following dosing scale:

	Insulin correction dose, U		
CBG, mmol/L	**Level 1 (insulin sensitive, incl. fasting)**	**Level 2 (usual patient)**	**Level 3 (insulin resistant, TDD >80 U)**
10.1 - 12.0	2	4	6
12.1 - 14.0	3	6	9
14.1 - 16.0	4	8	12
16.1 - 20.0	5	10	15
>20.0	6	12	18

To prevent insulin stacking, allow at least 4 hours between SC doses of insulin
Two-hourly dosing is acceptable intraoperatively
Reduce the basal doses to 80% of the usual dose on the night before and the morning of surgery
Omit prandial dosing while fasting
Provide hypoglycaemia management instructions wherever insulin is prescribed

Fig. 1. Basal-bolus insulin regimen.[16,25,26] (TDD = total daily dose; CBG = capillary blood glucose; SC = subcutaneous.)

on the management of these agents during the perioperative period is given in Table 2. Modification of oral therapy as the primary perioperative glycaemic control strategy is only appropriate in uncomplicated surgical patients who miss one meal during the perioperative period. Critically ill patients, those with poor glycaemic control and those who miss multiple meals, should be managed with an appropriate insulin regimen.[21,22]

Hypoglycaemia

The perioperative period represents an increased risk for undiagnosed hypoglycaemia while patients are fasting and under the influence of sedative agents. Whenever insulin is prescribed in hospital, hypoglycaemia treatment must be prescribed on the same chart. Perioperatively, a CBG <6.0 mmol/L should be interpreted as imminent hypoglycaemia. A CBG <4.0 mmol/L is associated with harm and must be treated. Interruption of insulin therapy is discouraged, but dose reduction may be necessary. Assess the patient with a low CBG for signs and symptoms of hypoglycaemia. Consider their feeding status (eating or fasting) and their risk of hypoglycaemia unawareness. Fig. 3 provides a suggested hypoglycaemia management algorithm. While under the influence of anaesthesia, treat all patients with a low CBG with intravenous dextrose. If the CBG is <6.0 mmol/L, administer 10 g intravenous dextrose; if the CBG is <4.0 mmol/L, give 20 g intravenous dextrose. Thereafter, the CBG should be measured every 15 minutes and treatment repeated until the blood glucose is corrected.[11]

Special circumstances

SC insulin infusion (SCII) (or insulin pump therapy) is increasingly used in the management of type 1 DM. Patients using an insulin pump should,as far as possible, maintain control of their own perioperative glycaemic management. When assessing these patients, consider the invasiveness, duration and site of the surgery, as well as the anticipated postoperative course. Question how many meals the patient will skip. Will the anaesthetist have access to the SCII intraoperatively? Will the device location infringe on the surgical site? Ideally, a preoperative basal test is done to establish glycaemic response to the fasting state. If this was not done, ask the patient to decrease the SCII to 70 - 80% of the basal rate while fasting. Ensure that the anaesthetic provider understands how to adjust, discontinue and remove the SCII if necessary. If continued intraoperatively, one or two small (2 - 4 U) SC correctional doses of insulin may be administered if the CBG rises ≥10.0 - 12.0 mmol/L. If this fails to correct the CBG, start a VRIII. If the CBG decreases to <4.0 - 6.0 mmol/L, treat the hypoglycaemia with intravenous dextrose. If hypoglycaemia persists, disconnect the SCII and switch to a VRIII. SCII is not appropriate for emergency surgery or where more than one meal is missed in the perioperative period.[23,24]

For patients with DM, day-case surgery must be considered.[14] It reduces the risk of iatrogenic complications and empowers the patient to manage their own perioperative glycaemic control. When assessing diabetic patients for day-case surgery, three aspects must be considered:

- Is the patient physically, mentally and socioeconomically capable to self-manage their DM and do they have easy access to emergency healthcare should they need it?
- Is their DM adequately controlled, with a recent HbA1c <8.5%?
- Is the nature of the surgery suitable for a day case?

A multidisciplinary context-sensitive approach

No single scenario describes every patient with DM who has to undergo surgery. At each facility (or group of facilities) a representative multidisciplinary team must evaluate the unique patient-resource environment and develop an evidence-based clinical practice guideline that fits their context. Smaller facilities should obtain input from their regional specialist centre.

It is essential to empower patients to self-manage their diabetes, especially in a setting where access to resources or healthcare personnel is limited. When appropriate, patients should be given guidance to manage their own insulin and non-insulin antidiabetic therapy in the ward.[21]

The dietician, or equivalent team member, must engage the kitchen service to ensure

Box 1. Alberti glucose-insulin-potassium infusion[21,27]

The GIK infusion is an alternative IV insulin regimen when a VRIII is not feasible. It provides substrate, IV insulin and electrolytes via a single infusion.

The original GIK regimen was published by Alberti and Thomas in 1979. It provides a safe and effective method of giving substrate, IV insulin in the same infusion. Alterations of the original regimen remain in use today.[28,29,30]

The original GIK regimen uses a bag containing 500 mL 10% dextrose and adds:

- 10 U short-acting insulin
- 10 mL 10% KCl.

The infusion runs at a fixed rate of 100 mL/h, providing 2 U insulin per hour.

CBG is measured 1 - 2-hourly. To increase or decrease the insulin infusion rate by 1 U/h the insulin content of the bag is changed up or down by 5 U. A new bag must be mixed each time it is decided to adjust the insulin infusion rate.

Problems with the GIK infusion are:

- labour intensive and wasteful when multiple bag changes are needed
- maintenance at 100 mL/h exceeds current standards for care of surgical patients
- 500 mL 10% dextrose bags are not available at all locations
- 10% dextrose water is not an acceptable maintenance fluid
- risk of DKA in type 1 DM if GIK infusion is stopped.

If deemed appropriate for the location, the local multidisciplinary team must adapt the GIK regimen to suite their context and address the concerns mentioned. Involve specialist input.

GIK = glucose-insulin-potassium; IV = intravenous; VRIII = variable rate intravenous insulin infusion; CBG = capillary blood glucose; DKA = diabetic ketoacidosis; DM = diabetes mellitus.

Use a dedicated IV access site and infusion set with an antireflux valve for glucose management
Add 50 U of regular short-acting insulin to 50 mL 0.9% NaCl (1 mL = 1 U)
Administer with a syringe driver connected to a port close to the dedicated IV cannula
Run dextrose-containing maintenance solution at 25 mL/kg/day (20 - 30 mL/kg/h range)
Monitor serum Na^+ and K^+ daily
Measure CBG hourly while the patient is under the influence of anaesthesia; 2-hourly if normoglycaemic, awake, attended, and not confused

	Insulin rates, mL/h		
CBG, mmol/L	**Level 1 (insulin sensitive, incl. fasting)**	**Level 2 (usual patient)**	**Level 3 (insulin resistant, TDD >80 U)**
<4.0	Reduce VRIII to 0.2 - 0.5 mL/h (stop VRIII if SC basal insulin continued) Administer 20 g dextrose IV Repeat CBG in 15 min		
4.1 - 6.0	Reduce VRIII to 0.2 - 0.5 mL/h (stop VRIII if SC basal insulin continued) Consider administration of 10 g dextrose IV to prevent CBG decreasing to <4.0 mmol/L Repeat CBG in 15 min		
6.1 - 8.0	0.5	1	2
8.1 - 12.0	1	2	4
12.1 - 16.0	2	4	6
16.1 - 20.0	3	5	7
20.1 - 24.0	4	6	8
>24.1	6	8	10
	Seek specialist advice		

Target CBG range 6.0 - 12.0 mmol/L. CBG up to 12.0 mmol/L is acceptable for a short period
Only increase VRIII if CBG remains high after 3 hours and is decreasing by <3 mmol/L/h
There is a risk of DKA when discontinuing a VRIII, as it creates a state of acute insulin withdrawal
Continue SC basal insulin while using a VRIII or administer SC basal insulin 30 min before discontinuing a VRIII

Fig. 2. Variable rate intravenous insulin infusion regimen.[21,22] (CBG = capillary blood glucose; IV = intravenous; TDD = total daily dose; VRIII = variable rate intravenous insulin infusion; SC = subcutaneous; DKA = diabetic ketoacidosis.)

Table 4. Blood glucose management according to feeding status

Feeding status	Management options
Eating normally	Modification of usual therapy or basal-bolus SC insulin with correction doses
Fasting	VRIII, modified Alberti's GIK, or basal insulin only*
Tube enteral feeding	VRIII, modified Alberti's GIK, or basal insulin only*
Total parenteral feeding	VRIII, modified Alberti's GIK, or basal insulin only*

SC = subcutaneous; VRIII = variable rate intravenous insulin infusion; GIK = glucose-insulin-potassium infusion.
*It is best to avoid short- or rapid-acting insulin, as there is an increased risk of hypoglycaemia. However, small correction doses with frequent monitoring may be required if glucose readings are >12 mmol/L.

Provide the diagnostic criteria and management of hypoglycaemia with every in-patient diabetes prescription
A low CBG must be interpreted in the context of the patient's feeding status and symptomatology
Decide whether the patient is at risk of hypoglycaemia unawareness. These include the frail, patients on beta-blockers, with long-standing DM, and those on medications with sedative effects. All such patients, including those under the influence of anaesthesia, should automatically be treated as symptomatic

CBG, mmol/L	Without symptoms and signs of hypoglycaemia		With symptoms or signs of hypoglycaemia	
	Normal diet	Fasting	Normal diet	Fasting
<4.0	Provide a snack and repeat the CBG in 15 - 30 min	Give 10 g dextrose IV and repeat the CBG in 15 - 30 min	Give 20 g dextrose IV and repeat CBG in 15 min Seek urgent help if no response to treatment	Give 20 g dextrose IV and repeat CBG in 15 min Seek urgent help if no response to treatment
4.0 - 6.0	Increase monitoring frequency	Repeat CBG within 30 min If persistent, give 10 g dextrose IV and increase monitoring frequency	Provide a snack and repeat CBG in 15 - 30 min	Give 10 g dextrose IV and repeat CBG in 15 min Seek urgent help if no response to treatment

Fig. 3. Management of perioperative hypoglycaemia. (CBG = capillary blood glucose; DM = diabetes mellitus; IV = intravenous.)

that the diabetic diet provides a constant caloric intake from meal to meal and day to day. This will reduce prandial fluctuations in blood glucose and reduce the need for correction doses of insulin. The surgical team should understand the meal plan to ensure that minimal time elapses from the start of preoperative fasting until the first postoperative meal.

The local protocol should consider how care will be escalated for selected patients. Every DM patient cannot be referred to a diabetologist. Also define how feedback on perioperative DM management will be used to bring the patient back into the primary healthcare system after the perioperative period.

Conclusion

DM is an ever-growing public health problem affecting patient outcomes after surgery. This article addresses the SA scope of the problem and provides a structure for managing the patient with DM presenting for surgery. A local multidisciplinary team should guide practice at each facility. The recommended reading section provides essential information for individual perioperative providers and teams caring for surgical patients with DM. Where a patient scenario falls outside the scope of this discussion, the provider must consult the local multidisciplinary team or referral specialist centre for guidance.

Key points

- DM is a modifiable risk factor of adverse surgical outcomes. Undiagnosed DM or an HbA1c >8.5% (69 mmol/mol) is an indication to postpone elective surgery.
- Monotherapy using SC short- or rapid-acting insulin according to a sliding scale is *not* recommended.
- In all patients with DM, attempt to minimise the starvation period to only one missed meal.
- A CBG range of 6.0 - 10.0 mmol/L is the recommended target in the perioperative period. A CBG up to 12 mmol/L may be acceptable.
- Safe insulin prescribing practice requires prescription of hypoglycaemia treatment on every insulin prescription chart.
- In-hospital interruption of insulin therapy is a common cause of DKA in patients with type 1 DM.
- A multidisciplinary team should drive context-sensitive perioperative management of DM.

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