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REVIEW

# Critical appraisal and systematic review of guidelines for perioperative diabetes management: 2011–2017

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## Abstract

**Purpose** To systematically evaluate the quality, consistency and the evidence support of guidelines for perioperative diabetes management.

**Methods** We retrieved guidelines through systematic search, critically evaluated their quality and compared the recommendations of included guidelines. Five aspects were compared: target level, management of hyper- and hypoglycaemia, frequency of monitoring, management of insulin, and management of oral anti-diabetic drugs (OADs).

**Results** Fourteen guidelines met our criteria, and 342 recommendations were extracted, the results of Appraisal of Guidelines for Research and Evaluation II (AGREE II) evaluation showed that none of the mean score in each domain was higher than 50%. On average, most guidelines had only one domain scored above 50%. Most recommendations (78.9%) did not specify their supporting evidence, 71 (20.8%) were formed using grading criteria, none cited systematic review or meta-analysis. Recommendations were inconsistent across different guidelines.

**Conclusions** The existing guidelines about perioperative management of diabetes needs improvement in methodology, as well as the production of evidence with high quality. Evidence-based guidelines are required for the perioperative management of diabetes.

**Keywords** Perioperative management · Diabetes · Clinical practice guideline · Systematic review · Quality assessment

These authors contributed equally: Xiaoyang Song, Jinjing Wang.

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## Introduction

Diabetes has become one of the most common chronic diseases threatening human health. According to the global report by the World Health Organisation, the prevalence of diabetes keeps rising. In 2014, 422 million adults were suffering from diabetes worldwide, which is four times higher than in 1980 (108 million) [1]. A study from the United States estimated that 20% of all patients undergoing surgery had diabetes [2]. Diabetes may affect the surgery in various ways. First, the surgery itself is a stressing factor, which imposes a negative effect on the patient's metabolic and endocrine status. Second, both the incidence of hyperglycaemia and hypoglycaemia are important risk factors in the perioperative period [3, 4]. Thus, an appropriate perioperative management is needed to avoid longer hospital stays and higher morbidity and mortality [4, 5].

Several institutions and organisations, including Association of Anaesthetists of Great Britain and Ireland (AAGBI), Joslin Diabetes Centre, Joint British Diabetes Societies (JBDS) and Chinese Medical Association (CMA), have developed guidelines for perioperative management of diabetes [6–9]. However, the quality of the existing guidelines, the consistency of recommendations and their supporting evidence remain unknown. In this article, we analysed and compared the recommendations and their supporting evidence from guidelines for perioperative management, and critically assessed their quality through Appraisal of Guidelines for Research and Evaluation II (AGREE II), a widely used guideline evaluation tool [10].

## Methods

### Data sources and search strategy

We systematically searched the following electronic databases: MEDLINE, Chinese Biomedical Literature Database (CBM), WanFang Data and China National Knowledge Infrastructure (CNKI). We also searched websites of Guidelines International Network (G-I-N), Scottish Intercollegiate Guidelines Network (NGC), National Guideline Clearinghouse (SIGN) and National Institute for Health and Clinical Excellence (NICE). We conducted a complementary search by Google to detect guidelines possibly missed by the systematic searches. We searched all sources from the date of their establishment until 31 December 2017. The detailed search strategy is presented in Appendix 1.

### Inclusion and exclusion criteria

We included all guidelines that were developed for the perioperative management of diabetic patients, other diabetic guidelines that contained recommendations on this topic were also included. The language was limited to Chinese or English and there was no limit on diabetes type and surgery type. We included guidelines published from 2011 to 2017. We excluded older version of guidelines if a later edition was available.

### Guideline selection and data extraction

Two researchers (X.Y.S. and Y.T.G.) conducted title and abstract screening, and then full text screening, independently of each other. Disagreements were solved by discussion. Four researchers (X.Y.S., Y.T.G., J.Y.Z. and X.T.M.) were divided into two groups and independently extracted following information of included guidelines: (1) basic information, including publication year, country, developing institution or organisation, amount of included recommendations, and grading criteria used for the quality of evidence and/or the strength of recommendations (if existed); (2) related recommendations and their supporting evidence.

### AGREE II evaluation

Four appraisers (X.Y.S., Y.T.G., J.Y.Z. and X.T.M.) assessed the quality of the included guidelines by AGREE II. The following six domains were assessed: scope and purpose, stakeholder involvement, rigour of development, clarity of presentation, applicability and editorial independence. Before the formal evaluation, two rounds of pilot evaluation were conducted to achieve better consistency.

### Comparison of recommendations

We compared the recommendations with regard to five aspects: target level, management of hyper- and hypoglycaemia, frequency of monitoring, management of insulin, and management of oral anti-diabetic drugs (OADs).

## Results

### Characteristics of guidelines

A total of 2008 references were retrieved by our initial search. Fourteen guidelines met our criteria [5–9, 11–19] and five of them [5–9] were specifically developed for the perioperative management of diabetic patients (Fig. 1). Nine countries were involved in the development of included guidelines. Table 1 presents characteristics of included guidelines.

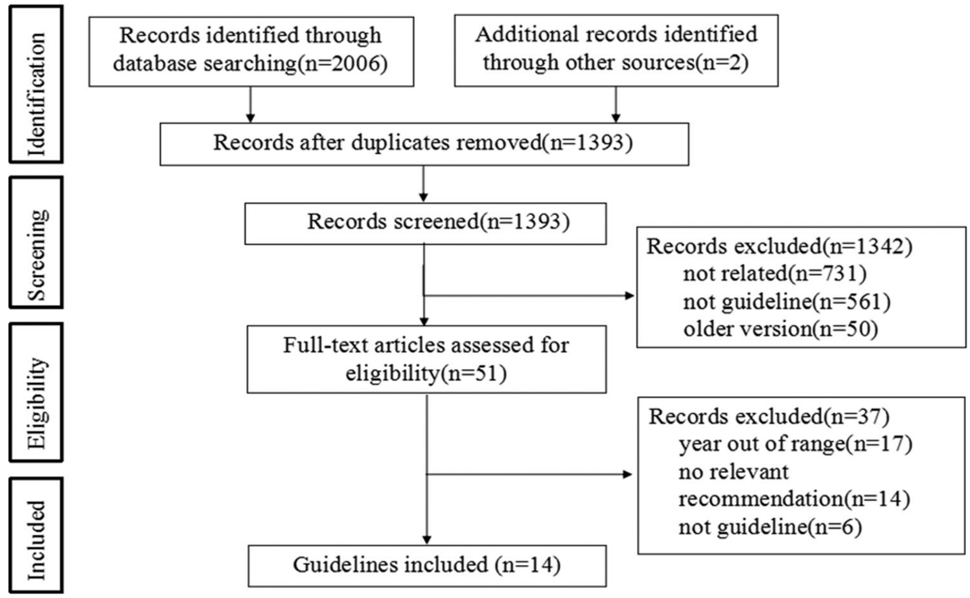


**Fig. 1** Flowchart of guideline selection. After selection, 14 guidelines addressing the perioperative management of diabetic patients were included

## AGREE II scores

After two rounds of pilot evaluation, the intra-class correlation coefficients in our formal evaluation reached 0.904 [95% confidence interval (0.848, 0.942)]. The results of our evaluation showed that the mean scores in all domains were <50%. The domain with the highest mean score (48.4%) were clarity of presentation and scope and purpose, and the domain with the lowest score (16.1%) was rigour of development. In most guidelines, only one domain had a score above 50%. Figure 2 presents the mean scores of the guidelines in each domain, and the evaluation results of each guideline is provided in Fig. 3, detailed items of AGREE II is presented in Appendix 2.

## Characteristics of recommendations

A total of 342 recommendations were included (Table 1). Seventy-one (20.8%) were developed in accordance with grading criteria, 36 (10.5%) applied the GRADE system [20] and 35 (10.2%) applied AACE protocol [21]. Of the recommendations using GRADE, 4 were supported by high, 10 by moderate, 18 by low and 1 by very low-quality evidence. Thirty-four recommendations were rated 'strong' and two recommendations 'weak'. For those using AACE protocol, recommendations with evidence levels from 1 to 4 were 10, 2, 0 and 10, respectively, and 25 did not provide the level of evidence; and recommendations graded from A to D were 20, 2, 0 and 13, respectively, and 22 did not provide grading. More details about the grading tools are presented in Appendix 2. In terms of supporting evidence, none of the included recommendations were supported by any systematic review or meta-analysis, up to 270 recommendations (78.9%) did not specify their evidence, and only 13 recommendations (3.8%) cited randomised controlled trials (RCT). Twenty-six recommendations were supported by other guidelines or consensus, 11 by observational studies and 3 by preclinical trials.

## Comparison of recommendations

### Level of blood glucose (BG)

Eight guidelines referred to target levels of BG (see Fig. 4). The recommended target range covered 5–12 mmol/L, but five did not provide their lower limit of target range. Three guidelines had support on their evidence from RCTs, another previously published guideline, or consensus, respectively.

### Level of HbA1c

Four guidelines gave recommendations in accordance with the level of HbA1c, a type of glycated hemoglobin that was formed when hemoglobin was exposed to blood glucose. Two guidelines gave an overall recommendation for the range of HbA1c, one guideline gave a recommendation for preoperative level and one guideline [17] for postoperative level. One guideline used a RCT as evidence, whereas the others used observational studies or other guidelines (see Table 2).

### Hyperglycaemia

Seven guidelines referred to the management of hyperglycaemia. All of them recommended insulin but the method

**Table 1** Characteristics of included guidelines

| Guideline | Country | Year | Institution/organisation | No. of recommendations |
|---|---|---|---|---|
| Guidelines developed for the perioperative management of diabetic patients | | | | |
| [5] | Australia | 2012 | ADS | 65 |
| [6] | U.K. | 2015 | AAGBI | 26 |
| [7] | U.S. | 2015 | Joslin Diabetes Centre and Joslin Clinic | 54 |
| [8] | U.K. | 2016 | JBDS | 83 |
| [9] | China | 2016 | CMA | 26 |
| Diabetes guidelines containing relevant recommendations | | | | |
| [11] | Australia | 2012 | ADS | 4 |
| [12] | U.S. | 2012 | Mayo Clinic | 25 |
| [13] | U.S., Belgium | 2012 | The Endocrine Society | 3 |
| [14] | U.S. | 2013 | AACE, TOS and ASMBS | 19 |
| [15] | Denmark, Norway, Sweden | 2013 | Copenhagen University Hospital, Oslo University Hospital, Uppsala University Hospital | 8 |
| [16] | U.S. | 2014 | Ohio State University Wexner Medical Center | 2 |
| [17] | India | 2014 | Base Hospital, S.C.B. Medical College, Central Railway Headquarters Hospital, A.G. Hospital and Jawaharlal Institute of Postgraduate Medical Education and Research | 16 |
| [18] | China | 2014 | CMA | 7 |
| [19] | China | 2014 | CMDA | 4 |
| Total | | | | 342 |

*ADS* Australian Diabetes Society, *JBDS* Joint British Diabetes Societies, *AAGBI* Association of Anaesthetists of Great Britain and Ireland, *CMA* Chinese Medical Association, *AACE* American Association of Clinical Endocrinologists, *TOS* The Obesity Society, *ASMBS* American Association of Metabolic and Bariatric Surgery, *CMDA* Chinese Medical Doctor Association

and situation differed. One guideline [8] recommended subcutaneous and intravenous insulin, the former for pre- and postoperative hyperglycaemia in patients with short starvation period, and the latter for patients whose surgery could not be delayed or response to subcutaneous insulin was inadequate. One guideline [5] recommended insulin–glucose infusion for intraoperative hyperglycaemia; another one [9] recommended subcutaneous insulin for non-critical patients and outpatients, and intravenous insulin for critical patients. None of the guidelines cited any supporting evidence (Table 3).

## Hypoglycaemia

Five guidelines mentioned the strategy of managing hypoglycaemia and provided recommendations, however, with differing level of details. Three guidelines [7–9] gave a detailed solution, mainly consisting of recommendations for assessing the patient's status, adjusting therapy and delivering the glucose. One guideline [6] only mentioned intravenous glucose in recommendations for hypoglycaemic patients. The guidelines mentioned above provided the dosage of glucose, while another guideline [11] only mentioned to halt insulin pump and start glucose infusion. In addition, none of these guidelines cited any supporting evidence.

## Frequency of BG monitoring

All five guidelines developed for the perioperative management of diabetic patients, as well as three other guidelines mentioned the frequency of BG monitoring (Table 4). Four guidelines recommended a frequency of once per hour, one guideline a frequency of once per 1–2 h and one guideline a frequency of once in 2 h, noting that the monitoring should be more frequent in special patients or special circumstances. Only three guidelines referred to supporting evidence. One [9] was based on other guidelines and consensus. The other two conducted quality assessment of evidence, finding that the quality of evidence was low [7] or that there was no evidence [17], but nevertheless both guidelines rated the strength of the recommendation high.

### Management of OADs

Nine guidelines discussed the management of OADs. Eight commonly used types of OADs (such as metformin) were mentioned. The most common strategy was to hold the drug. One guideline [8] stated that meglitinides and sulphonylureas should be omitted on the day of surgery. Another guideline [9] recommended that meglitinides and sulphonylureas should be held for 24 h before surgery and OADs should be held on the day of surgery. For patients undergoing short surgery, procedure and fasting was not required, it was not necessary to withhold drugs. Both of these two guidelines recommended that metformin should be omitted if the patient showed impaired renal function. One guideline [6] recommended the discontinuation of meglitinides and sulphonylureas on the day of surgery, whereas other drugs should be halted only when variable rate intravenous insulin infusion (VRIII) was to be used. Two guidelines [7, 18] only recommended to halt drugs preoperatively, without specifying the type of the drug. Two further guidelines [14, 19] suggested that after bariatric surgery, meglitinides and sulphonylureas should be held, other OADs could be halted or reduced when BG control was improved. One guideline [17] stated that the OADs were not recommended for use due to the lack of sufficient evidence.

Different guidelines had different recommendations concerning the circumstances under which the drugs should be discontinued on the day of the surgery. Two guidelines [6, 8] recommended that the morning dose of meglitinides was to be halted when the patient was nothing by mouth (NPO), and sulphonylureas should be halted in the morning when undergoing a morning surgery and be halted for a day in an afternoon surgery. One guideline [7] recommended to only hold the morning dose in spite of the surgery time. Only few recommendations cited any supporting evidence.

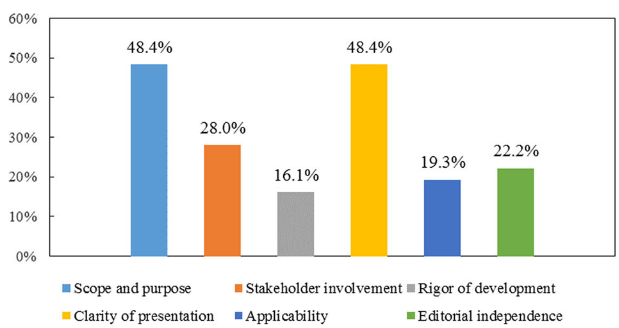


**Fig. 2** Mean scores in each domain. According to AGREE II instrument, six domains were evaluated, the rigour of development domain scored lowest, whereas clarity of presentation and scope and purpose domains scored highest

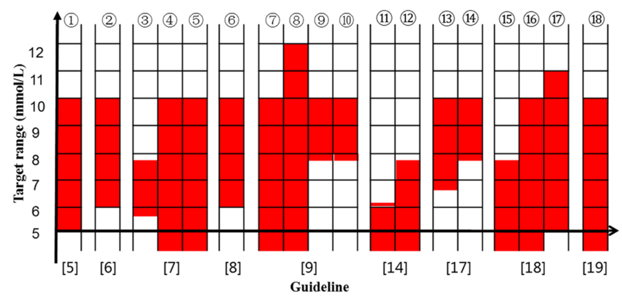


**Fig. 4** Target range of blood glucose. The period discussed in these guidelines varied. The recommended target range covered 5–12 mmol/L, five did not provide their lower limit of target range. One guideline only recommended the postoperative level of blood glucose, two guidelines presented the preoperative level and three guidelines did not specify the period. Note: (1) Blood glucose (BG); (2) capillary blood glucose (CBG), (perioperative); (3, 4) Non-critical, non-cardiac surgery patients: fasting blood glucose (FBG) or premeal BG (postoperative), random/bedtime BG (postoperative)#; (5) Cardiac surgery patients: BG (postoperative)#; (6) BG (postoperative), up to 12 mmol/L was acceptable; (7) FBG (preoperative)#; (8) Random or 2-h postprandial BG (preoperative)#; (9) BG (intraoperative); (10) BG (postoperative); (11, 12) Bariatric patient: FBG (preoperative)#, 2-h postprandial BG (preoperative)#; (13, 14) Patient undergoing coronary bypass surgery: enteral nutrition BG, parenteral nutrition BG; (15–17) Type 2 diabetic patient: FBG (preoperative)#; postprandial BG (preoperative)#, BG in major or moderate surgery (intraoperative); (18) Bariatric patient with type 2 diabetes: BG (preoperative)#. # Lower limit not provided

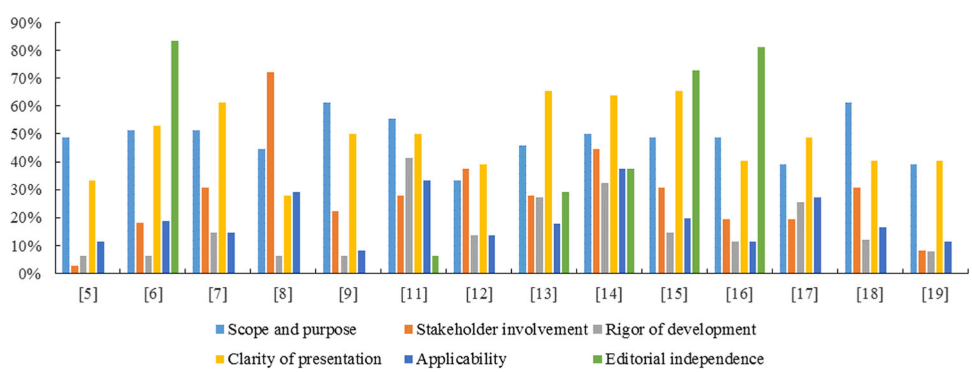


**Fig. 3** The evaluation results of each guideline. The score in each domain for each guideline was presented

**Table 2** Recommendations on HbA1c

| No. | Recommendation | Supporting evidence |
|---|---|---|
| [6] | Postpone elective surgery if possible when HbA1c ≥ 75 mmol/mol (9.0%) | RCT |
| [8] | Optimise glycaemic control, aiming for an HbA1c of < 69 mmol/mol (8.5%) before referral if possible, and if it is safe to do so. If HbA1c ≤ 8.5%, consider referral to the diabetes specialist team for advice if it is > 8.5% preoperatively | Observational study |
| [9] | A HbA1c level under 53 mmol/mol (7%) indicates low risk perioperatively. Postpone elective surgery when HbA1c > 64 mmol/mol (8%) | Observational study, guideline |
| [14] | Preoperatively: HbA1c 48–53 mmol/mol (6.5–7.0%) | Guideline |
| [17] | Patients well controlled on OADs with an HbA1c < 53 mmol/mol (7.0%) and without any intervention can be shifted to OADs after 7 days or at the time of discharge | Literature review |

### Management of insulin therapy

Nine of the included guidelines provided recommendations on the management of insulin therapy and focused on the circumstances under which insulin should be given, as well as the mode of delivery (Appendix 3).

The preoperative management was primarily focused on adjusting the delivery method and insulin dose. Two guidelines [8, 9] recommended to alter subcutaneous insulin to intravenous insulin, but the circumstances under which this should be done varied. Several guidelines suggested decrease or discontinuation of insulin under different circumstances, for example, five guidelines [5–9] recommended to hold short acting insulin, and reduce intermediate and long-acting insulin, with a decrease of 20–50%. One guideline [16] recommended to reduce preoperative evening dose of long-acting insulin by 20% for type 1 diabetes and by 50% for type 2 diabetes.

In intraoperative period, guidelines mainly focused on delivery method. For example, one guideline [8] suggested to start VRIII when BG was poorly controlled, another one [5] recommended to start insulin–glucose infusion before induction, and two guidelines [7, 18] suggested adjustment in delivery mode without providing the circumstance.

In postoperative period, guidelines focused on how to deal with the delivery method. Four guidelines [7–9, 18] recommended to alter the method when the patient was well enough to eat and drink, and two of them [8, 9] recommended to continue VRIII for 30–60 min after bolus dose in case of diabetic ketoacidosis.

## Discussion

Fourteen guidelines on perioperative management of diabetes were identified. We found that the methodology and reporting of included guidelines were unsatisfactory [22]. There were inconsistent recommendations across different guidelines, but we were still able to identify consistent management strategies.

The perioperative management of diabetes is focused on the BG control. An elevated HbA1c level indicates poor glucose management within 3 months, perioperative stress will make metabolic disorder worse under such circumstance [23]. Therefore, it is recommended that diabetic patients get HbA1c test preoperatively, and the management plan could be adjusted accordingly. Most of included guidelines believed that the target range of perioperative BG should be around 5–10 mmol/L, and a wider range (4–12 mmol/L) is acceptable depending on the patient's circumstance and the type of surgery. As for abnormal BG, perioperative hyperglycaemia can lead to higher risk of infections, cardio-cerebral vascular accidents, death, etc [24, 25]. This could be managed through insulin, if the capillary BG is higher than 10 mmol/L, intravenous infusion can be commenced until the BG is in control. Hypoglycaemia is deadly, it must be managed as quickly as possible [26]. It is necessary to monitor the BG level perioperatively in case of BG fluctuation, the frequency should be adjusted depending on BG level. As for medication, all the included guidelines recommended that OADs with high risk of hypoglycaemia should be halted preoperatively, metformin should be withheld under special conditions including kidney disease, liver failure and heart failure [27]. The management of insulin is vital, clinicians should focus on when and how to use insulin.

However, some recommendations were inconsistent in details. For the target range of BG, some guidelines [7, 8] stated that there was no need for a tight glycaemic control, since it did not promise a better outcome. Some guidelines recommended a narrow target range, some guidelines [14, 18, 19] only provided upper limit of BG. For OADs, some guidelines provided detailed recommendations for the discontinuation of different drugs, while others gave general recommendations to withhold them.

There was variability in recommendations on the management of insulin therapy as well, some guidelines provided a specific rate of infusion, whereas some only mentioned a decrease. For the injecting method, intravenous

**Table 3** Strategies for hyperglycaemia management

| No. | Time | Strategy | Supporting evidence |
|---|---|---|---|
| [8] | Preoperatively | Give rapid-acting analogue insulin subcutaneously, recheck the blood glucose 1 h later, if surgery cannot be delayed commence VRIII | None |
| [13] | Preoperatively | Discontinue noninsulin anti-diabetic agents and start insulin therapy | None |
| [5] | Intraoperatively: when BG > 10 mmol/L | Insulin–glucose infusion | None |
| [6] | Intraoperatively | Subcutaneous rapid-acting insulin should be given, a VRIII should be considered if a type 2 diabetic patient remains hyperglycaemic | None |
| [17] | Intraoperatively: BG > 10.0 mmol/L for 2 consecutive readings (hourly) | Start CIII | None |
| [8] | Postoperatively | Give rapid-acting analogue insulin subcutaneously, recheck the blood glucose 1 h later, if still above 12 mmol/L, repeat subcutaneous insulin dose after 2 h. Recheck 1 h later, if it is not falling commence VRIII | None |
| [9] | When BG > 10 mmol/L | Start insulin therapy, intravenous insulin is the first choice intraoperatively and in ICU postoperatively; subcutaneous insulin is for non-critical stable patients; for outpatient undergoing short surgery, rapid insulin is the first choice. Management plan should be individualised, low-dose and frequently monitored based on patients' situation for fear of hypoglycaemia | None |
| [16] | When BG > 10 mmol/L | Start insulin drip | None |

*VRIII* variable rate intravenous insulin infusion, *CIII* continuous intravenous insulin infusion

insulin, subcutaneous insulin and insulin–glucose infusion were recommended.

The differences in recommendations might arise from the clinical problems on which different guidelines focused, such as the situation of intended patients. Some guidelines were developed for a specific nation or area. It may also be attributable to the evidence base of included guidelines, as our results indicated, the majority of recommendations failed to cite supporting evidence and were formed through consensus. Recommendations should always be based on the best available evidence [28–32]. Recommendations supported by high-quality evidence were rare. Insufficient evidence may be the reason the inconsistency [7, 33], but the flawed methodology and the lack of systematic search may contribute to this as well. Systematic review or meta-analysis on perioperative management of diabetes might decrease such inconsistency [34]. Flawed methodology, and recommendations without reliable evidence might hinder the effective implementation of guidelines in clinical practice [31, 33].

The quality of methodology and reporting in the guidelines was poor. There were several ways to improve the methodology according to the items of AGREE II. Guidelines should define their PICO (patient, intervention, comparison, outcome) questions. Most of included guidelines need to consider patient's values and preferences. The included guidelines often lacked rigorous development methods: systematic literature searches should be conducted and reported, the existing available evidence should be retrieved and critically evaluated. Some guidelines failed to report the methods to formulate the recommendations and consideration on benefits and risks. Some should present the evidence to support their recommendations. The updating, target audience and external review should be mentioned. Some recommendations were mixed with other texts, and some did not include instructions on implementation. Moreover, the majority of the included guidelines did not present the competing interests of panellists, and how the funders and members with potential conflicts influence the guideline should be reported. The low quality of reporting makes it challenging for users to interpret, appraise, and apply those guidelines, and it might influence the implementation and dissemination of the guideline, leading to a waste of resources [28, 29, 33]. The production or collection of high-quality evidence, and following rigorous, reliable and evidence-based methodology, is necessary for the development of trustworthy guidelines. Although the guidelines included were imperfect, they are well used and helped with the standardised perioperative management of patients with diabetes [35].

**Table 4** Frequency of monitoring

| No. | Time | Frequency and recommendation | Supporting evidence |
|---|---|---|---|
| [7] | Perioperatively | Every 2 h, adjust the frequency based on BG level and surgery type | None |
| [5] | Intraoperatively | Hourly (at least): in major surgery | None |
| [8] | Intraoperatively | Hourly (at least), be more frequently if readings outside the target range | None |
| [9] | Intraoperatively | Every 1–2 h: general. Every 0.5–1 h: critical patients, patients under major surgery or intravenous insulin infusion. Every 15 min: in cardiopulmonary bypass operation. Every 5–15 min: when BG ≤ 3.9 mmol/L. Every 4–6 h: patients in starvation period | None |
| [12] | Intraoperatively | Hourly | None |
| [9] | Postoperatively | Hourly (at least): patients under intravenous insulin infusion | None |
| [6] | Not mentioned | Hourly, be more frequently if readings outside the target range | None |
| [17] | Not mentioned | Hourly for first 12 h and if blood glucose ranges from 7.2 to 10 mmol/L and fluctuation is < 10%, every 4 hourly for next 12 h: patients undergoing cardiac intervention | None |

## Strength and limitations

This is to our knowledge the first study that comprehensively explores both the quality and the contents of guidelines for perioperative management of diabetes. We performed a systematic literature search and critical evaluation and we evaluated the evidence support. AGREE II is a well-established and widely received tool [36, 37], we used it for evaluation. However, we found it hard to identify some recommendations and may thus have missed some: some recommendations were mixed with other texts, and some were not provided in the body of guideline.

## Conclusion

Our results indicate that the existing guidelines for perioperative diabetic management require improvement in methodology. The production of evidence with high quality and the development of evidence-based guidelines are needed for the perioperative management of diabetes.

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### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** This article does not contain any studies with human participants or animals performed by any of the authors.

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