Diabetes mellitus and perioperative outcomes: a scoping review of the literature

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Abstract

Background: Diabetes mellitus (DM) is frequently encountered in the perioperative period. DM may increase the risk of adverse perioperative outcomes owing to the potential vascular complications of DM. We conducted a scoping review to examine the association between DM and adverse perioperative outcomes.

Methods: A systematic search strategy of the published literature was built and applied in multiple databases. Observational studies examining the association between DM and adverse perioperative outcomes were included. Abstract screening determined full texts suitable for inclusion. Core information was extracted from each of the included studies including study design, definition of DM, type of DM, surgical specialties, and outcomes. Only primary outcomes are reported in this review.

Results: The search strategy identified 2363 records. Of those, 61 were included and 28 were excluded with justification. DM was mostly defined by either haemoglobin A1c (HbA1c) or blood glucose values (19 studies each). Other definitions included ‘prior diagnosis’ or use of medication. In 17 studies the definition was unclear. Type 2 DM was the most frequently studied subtype. Five of seven studies found DM was associated with mortality, 5/13 reported an association with ‘complications’ (as a composite measure), and 12/17 studies found DM was associated with ‘infection’. Overall, 33/61 studies reported that DM was associated with the primary outcome measure.

Conclusion: Diabetes mellitus is inconsistently defined in the published literature, which limits the potential for pooled analysis. Further research is necessary to determine which cohort of patients with DM are most at risk of adverse postoperative outcomes, and how control influences this association.

Keywords: blood glucose; complications; diabetes mellitus; glycated haemoglobin; postoperative complications; scoping review

Editor’s key points

- Diabetes mellitus is widely considered to be a risk factor for adverse postoperative outcomes, but it is not known whether this is true for all patients with diabetes mellitus.
- Diabetes mellitus is inconsistently defined in the literature and available studies report mixed associations between diabetes mellitus and postoperative outcomes.
- More work is warranted to identify the cohort of patients with diabetes mellitus most at risk of adverse outcomes by examining factors such as control of blood glucose.
Diabetes mellitus (DM) is frequently encountered perioperatively. Operations in patients with DM account for 15% of all procedures. Furthermore, up to 50% of patients with DM will require a surgical procedure during their lifetime. DM is largely divided into two main categories: type 1 DM (absolute insulin deficiency) and type 2 (insulin resistance and relative insulin deficiency), whereas in a minority diabetes is attributable to secondary causes, such as endocrine conditions and steroid use, or genetic disorders, including maturity onset diabetes of the young. However, the different types of diabetes are often discussed as a single entity and referred to as ‘diabetes’. This has the potential to cause confusion when developing guidelines for clinical practice. For example, guidelines mandating minimum fluid infusion rates have the potential to cause harm with respect to a patient’s overall fluid balance. To exemplify this, consider the patient with DM after major surgery who requires a variable rate insulin infusion for their glucose control, intravenous fluids with their patient-controlled analgesia system, an epidural infusion, and total parental nutrition. There are several insulin infusion regimes in use in current clinical practice, many of which evolved from research by Alberti and Thomas in the 1970s. Although there is solid clinical reasoning to use such methods for patients with type 1 DM, and in certain situations for patients with type 2 DM, developing and instigating guidelines requires careful consideration.

The long-term sequelae of poor glycaemic control in DM are increased risk of microvascular and macrovascular complications. A key concern for patients with DM undergoing surgery is increased risk of infection, which is thought to be secondary to modulation of immune response pathways. Postoperative complications such as infection can result in longer lengths of stay, higher re-admission rates, and inferior surgical outcome. Therefore, current guidelines focus on the association between poor glycaemic control in DM (defined as glycated haemoglobin A1c [HbA1c] >69 mmol L\(^{-1}\) or 8.5%) and adverse surgical outcomes. This has the potential to cause further confusion when studying this area — are all patients with DM at equal risk, or is glycaemic control the crucial factor? There is some evidence that if the diagnosis of DM is known before surgery, outcomes may be better. The current narrative is that DM is a risk factor for poor postoperative outcome, although no formal review has been undertaken in the noncardiac surgery literature to explore this concept.

Given the observational nature of this question and the heterogeneity of outcomes, it was decided that a scoping

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**Fig 1.** PRISMA flowchart demonstrating the full scoping review process from initial search to abstract screening and full text assessment. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.
Table 1 Summary of all papers included in the review. Data are grouped according to their primary outcome measure. *Not reported. AVf, arterio-venous fistula; CI, confidence interval; DM, diabetes mellitus; HD, haemodialysis; HR, hazard ratio; IGT, impaired glucose tolerance; IOP, intraocular pressure; IPTW, inverse probability of treatment weighting; JOA, Japanese Orthopaedic Association (Changes in motor, sensory and bladder function); LOS, length of stay; OR, odds ratio; PJI, prosthetic joint infection; QuickDASH, Quick Disabilities of the Arm, Shoulder and Hand (patient reported outcome measure assessing disability); RR, relative risk; SD, standard deviation; SSI, surgical site infection; UTI, urinary tract infection; WOMAC, Western Ontario and McMaster Universities Arthritis Index.

| Year | First author | Study design | # Patients (DM) | # Patients (control) | Surgical specialty | Primary outcome measure (mortality) | Reported differences between groups | DM associated with outcome |
|------|--------------|--------------|----------------|---------------------|--------------------|-------------------------------------|-----------------------------------|--------------------------|
| 2014 | Guzman64     | Retrospective cohort | 423 050 | 2 145 944 | Spinal | Mortality | OR=1.44; 95% CI, 1.19–1.74; P=0.0001 | Yes |
| 2014 | Guzman63     | Retrospective cohort | 223 908 | 1 378 237 | Spinal | Mortality | OR=2.08; 95% CI, 1.72–2.50; P<0.0001 | Yes |
| 2009 | Marchant52    | Retrospective cohort | 109 458 | 920 555 | Orthopaedic | Mortality | Controlled DM vs no diabetes: OR=0.855; 95% CI, 0.679–1.076; P=0.182 Uncontrolled diabetes vs no diabetes OR=2.700; 95% CI, 1.647–4.426; P<0.001 | Yes |
| 2015 | Lee54        | Retrospective case-control cohort | 419 | 2656 | Urology | All-cause mortality | OR=1.825; P=0.001 | Yes |
| 2015 | Zarrouk56    | Retrospective case-control cohort | 397 | 1709 | Vascular | Mortality | IPTW adjusted Cox regression (RR=0.98; CI, 0.75–1.29; P=0.91) | No |
| 2019 | Long54       | Retrospective cohort | 261 | 790 | Vascular | 30-day mortality | DM: 2.5% Control (glucose >180 mg dl⁻¹): 8.5% (P=0.02) | No |
| 2016 | Hjellestad57 | Prospective cohort study | 8 | 58 | Vascular | All-cause mortality | Multivariate Cox regression HR death=6.35; 95% CI, 1.49–27.1; P=0.01 | Yes |

| Year | First author | Study design | # Patients (DM) | # Patients (control) | Surgical specialty | Primary outcome measure (Composite measure of morbidity and mortality) | Reported differences between groups | DM associated with outcome |
|------|--------------|--------------|----------------|---------------------|--------------------|-------------------------------------|-----------------------------------|--------------------------|
| 2019 | Wysocki51    | Retrospective cohort | 343 | 1375 | General | Overall morbidity rate | DM: 7.27% Control: 5.58% Pre-diabetes: 6.64%; P=0.571 | No |
| 2019 | Guetta55     | Retrospective cohort | 143 | 841 | General | Mild complication (Clavien–Dindo classification <3a) | OR=2.32; 95% CI, 1.16–4.6; P=0.017 | Yes |
| 2015 | Reategui43   | Retrospective case series | 130 | 703 | Orthopaedic | Medical, infectious, mechanical, and surgical complications | –* | No |
| 2015 | Goodenough22 | Prospective cohort | 129 | 888 | General | Major complication using (Clavien –Dindo classification system) within 30 days of surgery | OR=1.17; 95% CI, 0.57–2.41; P=0.66 | No |
| 2019 | Law23        | Retrospective cohort | 104 | 104 | Orthopaedic | Complication rate | DM: 5.8% Control:4.8% | No |

Continued
| Year | First author | Study design | # Patients (DM) | # Patients (control) | Surgical specialty | Primary outcome measure (Composite measure of morbidity and mortality) | Reported differences between groups | DM associated with outcome |
|------|--------------|--------------|----------------|---------------------|-------------------|---------------------------------------------------------------------|----------------------------------|----------------------------|
| 2015 | Kallio⁵⁹     | Retrospective cohort study | 103 | 100 | Orthopaedic | Complication rate | DM (A1c <10%) + referral: 0.78 (1.01) DM no referral: 1.27 (1.18) No DM: 0.36 (0.63) (P=0.124) DM (A1c <8%) + referral: 0.50 (0.89) (P=1) | Yes |
| 2016 | Swirska⁷¹    | Retrospective cohort | 91 | 91 | Gynaecological | Number of perioperative complications (e.g. UTI, impaired wound healing) | OR=1.83; 95% CI, 0.68 −4.96; P=0.24 | No |
| 2006 | Hofmann⁵²    | Prospective cohort | 80 | 544 | Vascular | Periprocedural complications (fatal and non-fatal stroke, non-fatal myocardial infarction) | Inadequate control (HbA1c >7%) OR=3.7; 95% CI, 1.5−9.1; P=0.005 | Yes |
| 2012 | Myers⁵⁸      | Retrospective cohort | 74 | 74 | Orthopaedic | Any complication (infection, non-infection [e.g. non-union]) | OR=2.9; 95% CI, 1.42 −5.96; P=0.005 | Yes |
| 2018 | Kamarajah⁷⁷  | Prospective cohort study | 49 | 132 | General | Overall complications (Clavien−Dindo) | Multivariate logistic regression: OR≈2.08; 95% CI, 1.04−3.99; P=0.031 | No |
| 2020 | Law⁶⁷        | Retrospective cohort | 40 | 80 | Orthopaedic | Overall complication rate (infection, reoperation, non-union) | DM: 17.5% Control: 23.8% (P=0.489) | No |
| 2019 | Rudolph⁵⁴    | Retrospective cohort | 39 | 112 | General | Major complications Postoperative complications | DM: 53% (P=0.514) Multivariate logistic regression: OR≈1.042; 95% CI, 0.416−2.607; P=0.920 | No |
| 2016 | Bianchini⁵⁸  | Retrospective cohort | 31 | 137 | Head and neck | | | No |

| Year | First author | Study design | # Patients (DM) | # Patients (control) | Surgical specialty | Primary outcome measure (Infections) | Reported differences between groups | DM associated with outcome |
|------|--------------|--------------|----------------|---------------------|-------------------|-------------------------------------|----------------------------------|----------------------------|
| 2018 | Cancienne⁶¹  | Retrospective cohort | 13 470 | 103 586 | Orthopaedic | Deep infection within 6 months requiring debridement | DM: 0.33% Control: 0.19% (P=0.001) | Yes |
| 2019 | Lipsky⁵⁸     | Retrospective cohort | 4478 | 10 491 | Urology | Inflatable penile prosthesis infection | HR=1.32; 95% CI, 1.05−1.66; P=0.016 | Yes |
| 2013 | Kwon⁵⁶       | Retrospective cohort | 4098 | 7532 | General | Composite infections | Non-insulin DM: OR≈0.51; 95% CI, 0.37−0.69 Insulin DM: OR≈0.52; 95% CI, 0.35−0.76 | No |
| 2015 | Maradit Kremers⁵⁹ | Retrospective cohort | 3507 | 16 664 | Orthopaedic | PJI | HR=1.23; 95% CI, 0.87−1.74 | No |
| 2017 | Hoelzer⁵³    | Retrospective cohort | 452 | 2285 | Pain | Infection rate | DM: 1.99% Control: 2.54% (P=0.49) | No |

Continued
| Year | First author | Study design | # Patients (DM) | # Patients (control) | Surgical specialty | Primary outcome measure (Infections) | Reported differences between groups | DM associated with outcome |
|------|--------------|--------------|----------------|---------------------|-------------------|--------------------------------------|-----------------------------------|---------------------------|
| 2014 | Wukich⁵²     | Prospective cohort | 323            | 1737               | Orthopaedic       | SSI (within 30 days)                   | OR=3.99 (95% CI, 2.39–6.68)         | Yes                       |
| 2011 | Wukich⁵⁶     | Prospective cohort | 221            | 1241               | Orthopaedic       | SSI                                    | DM: 9.5% Control: 2.4% (P<0.00)      | Yes                       |
| 2017 | Rahimi-Nedjat⁵⁰| Retrospective cohort | 120            | 1254               | Maxillo-facial    | Infections                            | DM: 15.0% Control: 12.1% (P=0.383)   | No                        |
| 2014 | Fisichella¹³ | Retrospective case-control | 111           | 176                | Orthopaedic       | SSI                                    | OR=8.7                            | Yes                       |
| 1984 | Vannini⁴⁸    | Retrospective cohort | 47             | 1180               | Orthopaedic       | Deep phagosis (infection)              | DM: 11% Control: 2% (P<0.001)         | Yes                       |
| 2020 | Keavy⁹       | Retrospective cohort study | 43            | 321                | Gynaecological     | Infection                             | DM: 12.4% Control: 7.5% (P<0.05)     | Yes                       |
| 2006 | Liao³⁷       | Retrospective cohort | 39             | 298                | Spinal             | Infection                             | DM: 10.3% Control: 0.7% (P=0.003)    | Yes                       |
| 2014 | Hikata³⁸     | Retrospective case-control | 36            | 309                | Spinal             | SSI                                    | DM: 16.7% Control: 3.2% (P=0.0005)   | Yes                       |
| 2016 | Iavazzo³⁶    | Retrospective cohort | 34            | 266                | Gynaecological     | Infective complications                | DM: 32.4% (P=0.048) OR=3.5 (95% CI, 1.2–10.0) | Yes |
| 2008 | Olsen¹⁰      | Retrospective nested case-control | 29        | 199                | Orthopaedic        | SSI                                    | DM: 10.3% Control: 0.7% (P=0.003)    | Yes                       |
| 2013 | Motta¹³      | Prospective case-control | 28            | 18                 | Dental             | Clinical complications                 | Controlled DM: 7.7% Uncontrolled DM: 13.3% | No |
| 2010 | Ata³⁵        | Retrospective medical record review | —*            | —*                | General/vascular | Postoperative infection                 | Controlled DM: 7.7% Uncontrolled DM: 13.3% | Yes |

| Year | First author | Study design | # Patients (DM) | # Patients (control) | Surgical specialty | Primary outcome measure (specialty Specific) | Reported differences between groups | DM associated with outcome |
|------|--------------|--------------|----------------|---------------------|-------------------|---------------------------------------------|-----------------------------------|---------------------------|
| 2013 | Adams⁶⁰      | Retrospective cohort | 7567           | 32 924               | Orthopaedic       | Revision arthroplasty                        | HbA1c <7%, OR=1.32 (95% CI, 0.99–1.76) | No                        |
| 2013 | Takahashi⁶⁶  | Retrospective cohort | 41             | 124                 | Spinal            | JOA score                                   | DM: 22.7 (± 5.6) Control: 24.4 (± 4.2) (P=0.137) | No                        |
| 2000 | Kawaguchi¹⁴  | Retrospective case-control | 18            | 34                  | Spinal            | JOA score                                   | DM: 22.7 (± 5.6) Control: 24.4 (± 4.2) (P=0.137) | No                        |
| 2012 | Dokai¹⁹      | Retrospective case series | 13            | 65                  | Spinal            | JOA score                                   | DM: 22.7 (± 5.6) Control: 24.4 (± 4.2) (P=0.137) | No                        |
| 2017 | Brock²²      | Retrospective matched cohort | 100            | 100                 | Orthopaedic       | WOMAC scores (pain, stiffness, and physical function) | DM: 12.1 (7.7–16.5) Control: 12.4 (6.5–17.5) (P=0.578) | Yes                       |
| 2018 | Moazzeni¹⁶   | Prospective case-control | 48             | 48                  | Spinal            | Rate of Fusion at 1 yr                      | DM: 58% Control: 79% (P=0.02)         | Yes                       |
| 2018 | Sun³⁰        | Retrospective case-control | 11             | 141                 | Orthopaedic       | New onset or exacerbation of nerve symptoms | DM: 27% Normal glucose tolerance: 9% Impaired regulation: 19% (P=0.112) | No                        |
| Year | First author | Study design | # Patients (DM) | # Patients (control) | Surgical specialty | Primary outcome measure (Other including cardiovascular, renal, and LOS) | Reported differences between groups | DM associated with outcome |
|------|--------------|--------------|----------------|---------------------|-------------------|-----------------------------------------------------------------|-----------------------------------|-----------------------------|
| 2019 | Singh30      | Prospective cohort | 150            | 150                 | Ophthalmic        | Eye Complications (transient corneal oedema)                    | No                                | No                          |
| 1993 | Kodama34     | Retrospective cohort | 36             | 184                 | Ophthalmic        | Ophthalmic Complications (Macular Oedema and Transient elevation of intracocular pressure) | Yes                              | No                          |
| 2013 | Law36        | Retrospective case-control | 29            | 64                  | Ophthalmic        | Rate of qualified surgical success (IOP <15 and >5 mm Hg, without complications) | No                                | No                          |
| 2014 | Underwood46  | Retrospective cohort | 449            | 888                 | General/vascular  | LOS                                                            | Yes                              | Yes                         |
| 2018 | Lenguerrand40 | Prospective cohort | 64             | 523                 | Orthopaedic       | LOS                                                            | No                                | No                          |
| 2019 | Villamiel25   | Retrospective cross-sectional | 44            | 113                 | General            | LOS                                                            | No                                | No                          |
| 2013 | Bakker47      | Retrospective cohort | 329            | 1133                | Vascular          | 30-day cardiovascular complications                              | Yes                              | No                          |
| 2011 | Biterker71    | Retrospective cohort | 204            | 344                 | Mixed             | Postoperative cardiovascular events (PCEs)                      | Yes                              | Yes                         |
| 2017 | Shin73        | Retrospective cohort | 6034           | 48 811              | Spinal            | Acute renal failure                                             | Yes                              | Yes                         |
| 2008 | Feringa55     | Retrospective cohort | 69             | 220                 | Vascular          | Ischaemic Events                                                | Yes                              | Yes                         |
| 2012 | Afsar52       | Retrospective cohort | 73             | 160                 | Vascular          | Failure of AVF before first HD session                          | Yes                              | Yes                         |
| 2020 | Reinstatler20 | Retrospective cohort | 92             | 81                  | Urology           | 30-day postoperative visits for pain (ED or clinic)             | No                                | No                          |
| 2011 | Hwang31       | Retrospective cohort | 92             | 159                 | Urology           | Recurrence free survival in months                              | Yes                              | Yes                         |
| 2020 | Chung45       | Retrospective cohort | 67             | 538                 | Urology           | Post-void residual volume at 3 months (ml)                      | No                                | No                          |
| 2018 | Schroer55     | Retrospective cohort | 237            | 6107                | Orthopaedic       | Mean 90-day charges                                             | No                                | No                          |
| 2019 | Zimmerman57   | Retrospective cohort | 1503           | 9139                | Plastic           | QuickDASH score                                                 | No                                | No                          |
| 2008 | Tawil15       | Prospective case-control | 45             | 45                  | Dental            | Implant survival                                                | No                                | No                          |
review would be the best way to systematically map the literature to guide development of robust observational research in this area. Our scoping review is based on the following research question: Does existing literature support that DM is an independent risk factor for adverse perioperative outcomes?

We also explored the way DM is defined in the published literature and the current understanding of the relationship of control (defined by HbA1c level) and outcomes.

Methods

This scoping review was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, extended for use with scoping reviews.\(^\text{11}\) The protocol was developed before commencing the review and is available upon request from the corresponding author.

Literature search

An initial scoping search was performed using PubMed to collate relevant keywords and medical subject headings (MeSH). These were collated into a systematic search strategy combining free text and Boolean logic terms. The search was applied in CINAHL, the Cochrane library, MEDLINE, SCOPUS, and Web of Science. An example search strategy can be found in Appendix 1. The initial search strategy was developed with the assistance of an experienced Information Scientist (NK) in accordance with best practice guidelines.\(^\text{11}\) Reference lists of included studies and relevant reviews were also searched to supplement the systematic search. Where full texts were not available, we contacted the authors, which was successful in one case.

Eligibility criteria

The review question was specifically designed to address the epidemiology of outcomes for patients with DM and therefore studies investigating an intervention, such as RCTs, were excluded. Only manuscripts covering health-related outcomes, including patient-reported outcomes, were included. It was a prerequisite that papers included patients with and without DM undergoing elective, noncardiac surgery. We further limited the search to adult patients as the epidemiology of DM differs significantly between adult and paediatric patients.

Selection of studies

Duplicate references were removed using EndNote (EndNote, Clarivate Analytics). Manuscripts not available in English were also excluded at this stage. After removal of duplicates, studies were uploaded onto Rayyan (Rayyan Systems Inc. Online Software; available from: https://www.rayyan.ai/).\(^\text{12}\) As part of a consistent and comprehensive screening process two authors (DD and RB) screened all titles and abstracts independently to identify relevant studies for full text review. Rayyan collates a list of disagreements between the two authors, which were then examined by a third author (MA) to determine final inclusion.

Data extraction

The full texts identified for review were re-imported to a reference management software (EndNote, Clarivate Analytics). A screening and data collection tool was created a priori and tested (DD and RB) on the first 10 papers to assess suitability. All full texts were re-assessed against the key inclusion criteria and then relevant data was extracted using Microsoft Excel (Microsoft Corp., Redmond, WA, USA). Three authors were involved in data extraction (DD, RB, and CDF). Consensus was sought between the three extracting authors in cases of uncertainty. We recorded article characteristics such as design, statistical methods, Definition of DM, type of DM, participant counts, surgery types, and outcomes. Many studies looked at multiple outcomes. When it was not clear which was the primary outcome, we selected the outcome most applicable across different surgical specialities (i.e. mortality).

Data synthesis

Microsoft Excel was used to synthesise extracted data. We grouped studies based on the Definition of DM they used and the outcomes they studied, and value cut-offs for descriptors of glycaemic status. Frequencies were produced for the definitions studied, and we visually displayed these using a bubble plot. All included texts were synthesised into a single table to compare the outcomes studied.

Results

The systematic search produced 2363 records. After duplicates had been removed, 1714 title and abstracts were screened and 1625 excluded. The full text of 89 articles was assessed for eligibility. A total of 61 papers were included\(^\text{13–40,41–75}\) based on the predetermined criteria (described above). The remaining 28 articles were excluded with the reasons summarised in Fig 1. Table 1 summarises the included papers. Publication date ranged from 1984 to 2020. All studies used observational designs; most were retrospective designs with 12 studies utilising prospective methodologies. The range of patients with DM studied was from 8 to 214 944. The surgical specialties represented included: dental, spinal, vascular, ophthalmic, orthopaedic, urology, gynaecological, general, head and neck, and maxillo-facial.

Definition of diabetes mellitus used

The definition of DM used varied substantially as illustrated in Fig 2. HbA1c was used in 19 studies. A HbA1c of >6.5% was the most common cut-off applied in five studies. Notably, in one study HbA1c values within the preceding 1–2 yr before study were accepted as diagnostic.\(^\text{65}\) In the 19 studies reporting blood glucose, a range of diagnostic methods were reported including random, fasting, and glucose tolerance tests. In one study, diabetes mellitus was self-reported as part of the functional co-morbidity index, which was later corroborated against participants’ medications. They found all patients had correctly reported their status but were unable to distinguish between type 1 and type 2 DM.\(^\text{66}\) In 17 studies the definition was unclear, or not reported in the manuscript. In six cases, DM was defined by use of hypoglycaemic agents. Three studies specifically referenced international guidelines (WHO and American Diabetes Association).

It was not always clear which type of DM was being studied. Forty studies specified DM, but not which type. Five studies used “Type 1 and Type 2” to classify DM. In nine studies patients with type 1 DM were excluded, and only type 2 DM was
studied. In one study the registry from which patients were identified contained 98% patients with type 2 DM but the analysis was done using presence vs absence of DM. Fourteen studies subclassified DM by control. Of these, 11 used HbA1c to define control. Cut-offs included 6.5%, 7%, 8%, 7–9%, 8–9%, and 47 mmol mol⁻¹. The remaining three used International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes which are linked with complications (such as ophthalmic manifestations). Other ways of subcategorising patients included by management. For example, insulin-us non-insulin-dependent DM was found in four studies. Overall, there was no consistency in the way DM or control of DM was defined.

Outcomes studied

Table 1 outlines the primary outcomes studied. Some studies used outcomes that would be applicable to all surgical specialties (i.e. mortality and length of stay), whereas others used outcomes specific to a surgical specialty (e.g. Japanese Orthopaedic Association [JOA] scores and need for revision arthroplasty). Seven studies analysed mortality and found that DM was associated in five cases. Mortality was analysed within different timescales including: inpatient, 30-day, and longer term (up to 8 yr). In one study mortality was included as part of a composite measure ('adverse postoperative outcomes'). In 12 studies perioperative complications were analysed as a group, as a composite measure. Patients with DM experienced higher rates of complications in five of these studies. Infection was analysed in 17 studies. Like mortality, infective outcomes were not consistently defined.

Definitions of infection included surgical site infection, unrelated infection (such as urinary tract, or pulmonary), and operation specific infection (prothesis infection). Infection was frequently included in composite outcomes. Where it was the primary outcome, DM was associated with postoperative infection in 12 cases.

Of the 60 papers included in this scoping review, 33 reported that DM was associated with their primary outcome measure. Often multiple outcome measures were studied; this meant that DM may have been associated with one outcome, but not another in the same study.

Discussion

This scoping review is the first of its type to examine the existing literature studying the relationship between DM and adverse perioperative outcomes in the noncardiac surgery literature. Understanding this relationship is important for guiding future research in this area and identifying where targeted interventions will benefit patients most. This is increasingly important as the burden of DM increases among surgical patients.

Variable definition of diabetes mellitus

Through the systematic search of the available literature, we found that DM is defined in multiple ways: using HbA1c values, blood glucose investigations, patient records, and prescribed medications. Furthermore, the cut-offs applied for the Definition of DM, and glycaemic control varied substantially. Such inconsistencies have the potential to undermine

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**Fig 2.** Bubble plot of diabetes mellitus definitions. Bubble plot depicting the range of definitions used in the published literature studying the association between diabetes mellitus and adverse postoperative outcomes. *OGTT, oral glucose tolerance test. HbA1c, haemoglobin A1c.*
the value of pooled analyses. It may be possible to perform a
systematic review and meta-analysis with the existing litera-
ture, but it would require asking a well-formulated question,
focusing on just one of the outcome measures such as mor-
tality or infection, which both have studies addressing them
with thousands of patients included. However, to take mort-
ality as an example, caution would be necessary as all seven
studies from this scoping review used a different definition of
DM.

In addition, variable definitions and cut-offs may cause
cfusion when discussing glycaemic control. This is an
important consideration for the perioperative multi-
disciplinary team who need to communicate with diabetes
specialists, support preoperative optimisation, and decide
whether it is appropriate to proceed with an operation. The
American Diabetes Association have published consensus
guidelines advising the use of hyperglycaemia, hypo-
glycaemia, time in range, and diabetic ketoacidosis as clini-
cally meaningful outcomes measures in type 1 DM, which
could be modified for use in type 2 DM.

Limitations of HbA1c
Existing guidelines focus on HbA1c as a marker of glycaemic
control. HbA1c gives an average of control over 2–3 months
and is widely used because of its low costs and reproducibility
of measurement. However, literature studying type 1 DM
highlights its limitations, specifically its inability to assess
short-term glycaemic variability (GV) and its inability to
quantify hypoglycaemic burden. Moreover, HbA1c is inaccu-
rate in patients with anaemia or abnormalities in renal func-
tion, both of which are common in surgical patients, limiting
the value of HbA1c in this setting. Short-term GV, as
measured with continuous glucose monitors, was not studied
in any of the papers found in this scoping review. Incorpo-
rating short-term measures of GV are an important consider-
ation for future perioperative research with a potential role in
aiding preoperative optimisation but also improved care dur-
ing a hospital stay by enabling patient autonomy and closer
monitoring for complications such as hypoglycaemia. Numerous alternative novel biomarkers for
DM diagnosis, control, and complications are currently being
explored. Micro-RNAs are currently being studied as potential
biomarkers for the early detection of DM and its associated
complications. Although scientific and methodological bar-
riers remain before they can be implemented in clinical
practice, they show promise and may be relevant to periop-
erative practice in the next decade.

Outcomes studied
On the question of whether DM is a risk factor for adverse
perioperative outcome, the answer is patient, operation, and
perioperative outcome specific. This scoping review reports
primary outcomes, but most papers studied multiple out-
comes and many reported associations with some – but not all
– outcomes. Interestingly, the four largest studies (>10 000
patients with DM) found an association between DM and their
primary outcome measure. For the remaining studies, no
trends were seen between study size and likelihood of a
detected association. No further trends were noted between
factors such as methodology or DM Definition and outcomes.

The outcomes found in this scoping review can be classified
as either (1) generalisable to the whole surgical population or
(2) specific to certain surgical specialities. In terms of outcomes
relevant to all surgical patients, such as mortality, the litera-
ture reports an association in most cases, but not all. Similar
mixed findings were reported for length of stay (LOS), infec-
tion, and composite complication measures. For specialty-
specific measures, no differences were seen between groups
in studies using the JOA score, but significant differences were
found for ophthalmic and vascular complications, which is
unsurprising given the micro- and macro-vascular complica-
tions associated with DM. The need for consistent definitions
for seemingly dichotomous variables such as mortality has
been discussed elsewhere. This review corroborates those
observations with studies using various mortality endpoints
(in-patient vs 30-day mortality). We support the call for
standardised endpoints in observational studies.

Role of complications of diabetes mellitus related to
outcome
It is important to distinguish between definitions of DM con-
control. Many of the studies included in this review specifically
referred to glycaemic control (HbA1c), but well-controlled DM
refers to more than just a glycaemic marker such as HbA1c. It
may include factors such as blood pressure, weight, or lipid
status. Three studies had used ICD-9-CM codes to stratify their
groups by control, which include reference to microvascular
complications. A closer examination of the association
between presence of DM complications and perioperative
outcomes would be of value in future research. This has been
explored by our group in colorectal cancer, suggesting that
presence of complications is associated with both post-
operative mortality (90-day) and death during the surgical
episode.

Conclusions
In conclusion, robust observational studies are warranted to
further expand our understanding of the relationship of DM to
adverse postoperative outcomes. This will be aided by
consistent definitions and considering a wider perspective on
DM control, including GV and complication status. Defining
cohorts of patients with DM who are most at risk will allow
implementation of targeted intervention to improve
outcomes.

Authors’ contributions
Conceptualisation: DJD, RJB, SH, RA.
Methodology: DJD, RJB, SH, RA.
Formal analysis: DJD, RJB, CDSF, MA.
Investigation: DJD, RJB, CDSF, MA.
Writing of original draft: DJD, RJB.
Writing, review, and editing: DJD, RJB, CDSF, MA, SH, RA.
Visualisation: DJD, RJB.
Supervision: SH, RA.

Funding
National Institute for Health Research (to DJD, an Academic
Clinical Fellow).
Declarations of interest
SH is a director of the British Journal of Anaesthesia and is a member of the editorial board.

Acknowledgements
N. King (University of Leeds) helped to build the first iteration of the systematic literature search.

Appendix A. Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2022.02.013.

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*Handling editor: Jonathan Hardman*