Pilot and Feasibility Studies

RESEARCH

Open Access

Feasibility of a prospective multicenter observational study—is diabetes a risk factor in ERAS joint arthroplasty?

Luma Mahmoud Issa[1,2*], Christoffer Calov Jørgensen[2,3], Sten Madsbad[4], Martin Lindberg-Larsen[2,5], Claus Varnum[2,6], Thomas Jakobsen[2,7], Mikkel Rathsach Andersen[2,8], Manuel Josef Bieder[2,9], Søren Overgaard[2,10,11], Torben Bæk Hansen[2,12], Kirill Gromov[2,13] and Henrik Kehlet[2,14]

Abstract

Background Diabetes mellitus is a surgical risk factor, yet perioperative diabetes management remains debated, with inconsistent guidelines and limited consideration on the implementation of "enhanced recovery after surgery" (ERAS) programs. A detailed prospective observational multicenter study was launched to investigate perioperative risk factors and outcomes in diabetic patients undergoing modern optimized hip and knee arthroplasty within an established ERAS program.

Methods This study reports on the feasibility of launching prospective detailed observational studies as part of daily clinical practice within a multicenter collaboration, focusing on data completeness and successful recruitment.The feasibility analysis was conducted from October 1, 2022, to January 31, 2024, across eight public arthroplasty centers in Denmark, in diabetic patients undergoing elective primary total hip (THA), total knee (TKA), or unicompartmental knee (UKA) arthroplasty. Prospective data collection included antihyperglycemic medication, preoperative HbA1c, data on perioperative diabetes management, length of stay (LOS), and readmission after surgery.

Results The cohort comprised 1007 DM patients (37.6% ($n=379$) THA, 44.5% ($n=448$) TKA, 17.9% ($n=180$) UKA) with a mean age of 70.7 years (SD 8.8), and the median age was 71 (IQR 65–77); 48% were female and 19% were insulin-treated. Data on the type of preoperative antihyperglycemic medications was available in 100% of patients. LOS was registered in 100% of patients, and 90-day follow-up was completed in 99% of patients. Preoperative HbA1c assessment increased from 68% in February 2023 to 96% in January 2024. From March 1st, 2023, data on perioperative diabetes management was available for 98% of all patients, with a total completion variation between 94 and 96% across the included parameters.

Conclusion The study demonstrates the feasibility of a prospective multicenter setup for detailed data collection on diabetic patients undergoing ERAS hip or knee arthroplasty. The high compliance rates of key metrics (≥ 94%) support that data completeness and quality are sufficient to proceed with the main study to assess the impact of diabetes and its management on outcomes within an ERAS program in 2000 patients, since enrollment exceeded expectations.

*Correspondence:
Luma Mahmoud Issa
luma.mahmoud.issa@regionh.dk
Full list of author information is available at the end of the article

Trial registration ClinicalTrials.gov. NCT05613439. Registered on 9 January 2022, https://clinicaltrials.gov/study/NCT05613439?id=NCT05613439&rank=1

Keywords Diabetes, Joint surgery, Enhanced recovery, Complications

Key messages regarding feasibility

- What uncertainties existed regarding the feasibility?

Is it possible to design a multicenter, prospective observational study with effective collection of detailed data on perioperative diabetes management and outcomes as part of routine clinical practice in ERAS hip and knee arthroplasty?

- What are the key feasibility findings?

Perioperative enrollment and data collection rates of ≥ 94% confirmed sufficient data completeness and adherence to the ERAS framework in diabetic patients.

- What are the implications of the feasibility findings for the design of the main study?

The successful data collection and high compliance rates demonstrate the feasibility of this study design and support proceeding with the main trial to evaluate the impact of diabetes management on outcomes within an ERAS framework. The concept of detailed prospective studies nested within routine ERAS frameworks can be applied to other patient-groups and procedures, thereby guiding future large-scale clinical trials and guidelines.

Introduction

There is a general agreement that diabetes mellitus (DM) is a risk factor for prolonged hospital stay and postoperative complications in surgical patients [1–5]. Meanwhile, perioperative diabetes management remains highly debated [6, 7].

Standardized enhanced recovery after surgery (ERAS) programs have been shown to facilitate recovery, decrease postoperative complications [5, 8] and reduce postoperative disturbances in glucose homeostasis [9, 10]. Although the overall role of DM as a preoperative risk factor has been investigated in some studies within ERAS hip and knee arthroplasty [5, 11–13], the combined clinical challenges and results in relation to perioperative diabetes management have not. Thus, the impact of diabetes as a preoperative risk factor and its perioperative management within a well-established ERAS framework remains controversial [13]. Although a classical RCT has been a gold standard for previous trials, newer developments have included cluster randomized trials, platform trials, etc., in order to decrease costs and study duration. However, future studies should be performed within an ERAS framework to provide conclusions based upon optimized treatment protocols, thus minimizing confounding factors and morbidity risk related to traditional care [14].

Consequently, a Danish national prospective observational study in patients with DM undergoing hip and knee arthroplasty within an established improved ERAS framework has been protocolized [15]. In this protocol, it was estimated that at least 1400 hip and knee arthroplasty patients with DM were needed to demonstrate a reduction in patients with length of stay (LOS) of more than 4 days or 90-day readmissions of 3% compared to an earlier study within the same setup [5, 15].

Several outcomes have been predefined, including the proportion of DM patients with LOS > 2 and > 4 days, readmission rates, the association between perioperative diabetes treatment and outcome, the specific role of perioperative management of glucagon-like peptide-1 receptor agonist (GLP-1RA) and sodium-glucose cotransporter-2 inhibitor (SGLT2-i) in patients with DM, and achievements of same-day discharge in hip and knee arthroplasty in patients with DM [15].

The present study is a report on the feasibility of the planned ambitious data collection during the initial 16 months of this protocolized observational multicenter study nested within a routine clinical ERAS framework [15]. The results may be useful for future planning of similar investigations in patients with other complex preoperative comorbidities on a procedure-specific basis and within an ERAS framework.

Objectives

To assess the feasibility of the initiated trial design as part of routine clinical practice within the planned prospective observational framework [15]. Feasibility was defined a priori based on two domains: data completeness and patient recruitment. The primary outcome was the completeness of perioperative data related to diabetes status and perioperative management. Secondarily, we evaluated whether overall recruitment progressed as planned.

Methods

Study design

This was a non-randomized study evaluating the feasibility of continuing the ongoing large-scale cohort study in relation to the viability of the design and workflow for recruitment and datacollection [15]. Interim analyses were performed after every 400 patients to ensure recruitment, data availability, and process implementation across centers before proceeding to the main analyses.

Setting

The Center for Fast-track Hip and Knee Replacement consists of 8 public arthroplasty centers across all 5 regions in Denmark, covering about 40% of the annual number of arthroplasties in Denmark [16, 17]. Perioperative diabetes care followed local guidelines [7].

Sample size considerations

No formal power analysis was performed, but we aimed to have included about half of the planned patients for the main study at the time of analysis. This would accommodate for initial difficulties with data collection and allow for prolonging the inclusion period of the main study if necessary. Based upon an expected average of 900 patients/year/department and with a 10% incidence of diabetes, 1 year of data collection was necessary to include 720 patients. As data collection was gradually expanded throughout the study period, we decided to use all available data from the introduction of data collection in 2022 and until 10 months of complete diabetes-specific data registration, which was initiated in March 2023.

Statistics and reporting

Descriptive statistical analyses were conducted in IBM SPSS statistics version 29.0.1.0, and figures were created in Excel. Reporting adhered to the STROBE guidelines recommended for feasibility studies in preparation for large-scale cohort studies [18]. A level of completeness of > 90% for each of the collected variables was considered as confirming the feasibility of data collection, while a recruitment rate of > 750 patients was considered to confirm the feasibility of patient recruitment for the main trial.

Study population

The study period was from October 1 st, 2022, until January 31 st, 2024, and included patients with DM receiving an elective primary total hip (THA), total knee (TKA), or unicompartmental knee (UKA) arthroplasty registered in the database and consenting to data collection and follow-up. All surgeries were performed within an established ERAS program [16].

Data sources

Data was prospectively collected by dedicated research staff at the individual study sites and stored online in a REDCap database [19] in collaboration with the Open Patient data Explorative Network (OPEN) at Odense University Hospital. All outcome data were registered by the research staff and based on the unique Danish hospital register system securing complete follow-up.

The database includes information on LOS and 90-day follow-up on readmissions for all patients, while the type of antihyperglycemic treatment and preoperative HbA1c were collected specifically for patients with DM from October 1 st, 2022. Since recommendations on perioperative DM management initially differed due to the lack of evidence [7], data on perioperative diabetes management were registered from March 1 st, 2023. This included cessation and reuptake times for antihyperglycemic treatment, data on the use of GI/GIK and insulin administrations in hospital, the preoperative dose of glucocorticoid, the last measured blood glucose before discharge, and the time of surgery before or after 12:00 PM.

Results

The study cohort included 1007 patients with diabetes, drawn from a population of 9,618 consecutive patients out of the initially planned 1400 patients with diabetes undergoing hip or knee arthroplasty (Fig. 1). The overall inclusion rate was 96.3% of all operated patients in the centers, only excluding 3.7% who did not give consent to be registered in the database. Of patients with DM, 379 (38%) had THA, 448 (44%) had TKA, and 180 (18%) had UKA. The mean age was 70.7 (SD 8.8) years (median 71 (IQR 65–77)) and 48% were females.

Registration of antihyperglycemic medication was complete in 100% of patients. Of these, 815 (81%) patients received treatment with other antihyperglycemic medications than insulin, 157 (15.5%) patients were treated with insulin in combination with other antihyperglycemic medications, and 35 (3.5%) patients were treated with insulin alone. Antihyperglycemic medication was divided into 6 pharmacological groups, with 79% of patients being treated with metformin, 40% with GLP1RAs, 28% with SGLT2is, and 19% with insulin (Fig. 2). LOS was registered in 100% of patients, and 90-days follow-up was completed in 99% of patients.

By February 1 st, 2023, 68% of all patients with diabetes had their HbA1c taken prior to surgery but gradually optimized, resulting in 96% registration of preoperative HbA1c measurements at the end of

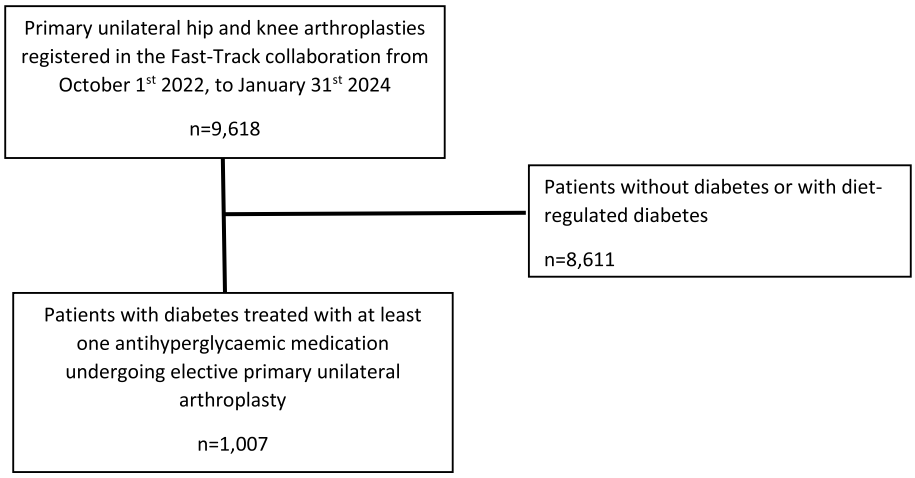

Fig. 1 Diagram of the study population

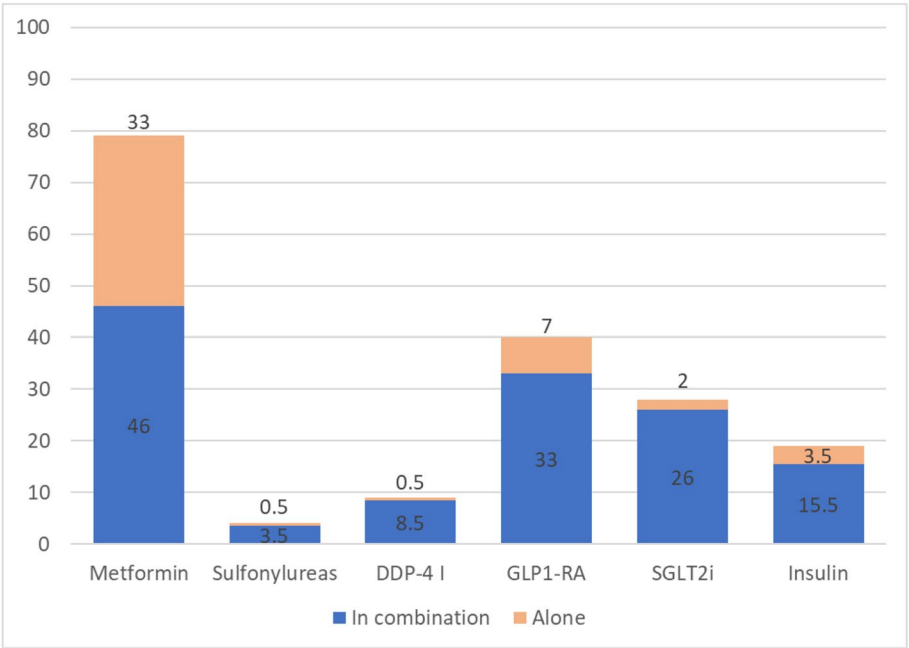

Fig. 2 Distribution of antidiabetic treatments, alone or in combination, in diabetic patients undergoing hip or knee arthroplasty between October 1 st 2022 and January 31 st 2024 ($n = 1007$). Abbreviations: DDP-4i, dipeptidyl peptidase-4 inhibitor; GLP1-RA, glucagon-like peptide-1 receptor agonist; SGLT2i, sodium-glucose co-transporter-2 inhibitors

inclusion across all centers, with a variation in centers between 92 and 100% (Table 1). Similarly, data on perioperative diabetes management were implemented and available for at least one of the defined parameters in 98% of patients across all centers from March 1 st, 2023, with the completeness for the individual parameters ranging from 94 to 96% across all centers (Table 1). All key parameters demonstrated only minor variation between the participating departments (Table 1).

Discussion

The results of the present feasibility study in 1007 patients with DM undergoing hip or knee arthroplasty in a large prospective multicenter study demonstrate the detailed perioperative assessment in ≥ 94% of patients. Thus, our data support proceeding with the main study without major protocol modifications [15]. Compared to the international literature [1, 2, 6, 12, 13], the study is unique by introducing standardized perioperative care as a part of the ERAS regimen [15]

Table 1 Completeness of preoperative data on type of antidiabetic treatment, length of stay, 90-day follow-up, pre-operative HbA1c and perioperative diabetes management (see legend) overall and by site

Data	Total %	Site A %	Site B %	Site C %	Site D %	Site E %	Site F %	Site G %	Site H %
Patients included after 01.10.22[a]	*n* = 1007	*n* = 123	*n* = 13	*n* = 201	*n* = 216	*n* = 111	*n* = 186	*n* = 113	*n* = 44
Antihyperglycemic medicine	100	100	100	100	100	100	100	100	100
Length of stay	100	100	100	100	100	100	100	100	100
90-day follow up	99	98	100	100	100	98	99	100	100
Patients included after 01.02.23[a]	*n* = 790	*n* = 94	*n* = 13	*n* = 156	*n* = 170	*n* = 82	*n* = 151	*n* = 85	*n* = 39
Preoperative HbA1c	96	100	100	92	98	94	95	100	95
Patients included after 01.03.23[a]	*n* = 726	*n* = 83	*n* = 13	*n* = 141	*n* = 161	*n* = 72	*n* = 140	n = 80	*n* = 36
Perioperative diabetes management—total[b]	98	99	100	96	98	93	100	100	100
Data on cessation and reuptake time for antihyperglycaemic treatment	95	98	100	95	89	90	100	100	100
Data use of GI/GIK and sliding scale insulin in hospital	96	99	100	96	88	93	100	100	100
Data on perioperative steroid administration	94	98	100	94	98	90	99	79	83
Data on discharge blood glucose	94	98	92	96	98	90	99	80	89
Time of surgery	96	98	100	96	98	90	100	90	89

[a] The completeness of each variable was calculated separately for patients enrolled after 01.10.2022, 01.02.2023, and 01.03.2023, as indicated in the table

[b] Perioperative diabetes management—total included data on one or more of following: ceasing or reuptake time for antidiabetic treatment, use of GI/GIK or sliding scale insulin in hospital (yes/no), discharge blood glucose (yes/no), use of steroid (yes/no), surgery time (before or after 12 am)

which may be important due to documented reduction in postoperative morbidity [8, 20], insulin resistance, and glucose homeostasis disturbances by ERAS [9, 10].

Also, the study will add to the current discussion on several important aspects regarding preoperative use of glucocorticoids in diabetic patients, especially with regards to dosing, insulin-dependent diabetes, and preoperative dysregulation [12].

The main study was planned to include 1400 patients, but recruitment exceeded expectations, allowing the expansion of the cohort to 2000 patients within the scheduled timeframe. This may provide a reliable and valuable contribution to future guidelines for patients with DM undergoing a relatively major operation within a fully implemented ERAS program.

In relation to the feasibility of undertaking such detailed data collection into a scientific database, we found that it took 4 months to get 96% completion of preoperative HbA1c measurement from initially 68% (February 1st, 2023) and 3 months to achieve data on perioperative diabetes management in 98% of all patients, with a total completion variation between 94 and 96% across the included parameters. This seems a relatively short time considering the current database prospectively collects a multitude of other preoperative and outcome-related data [16, 17]. Thus, our setup may be encouraging for others to perform similar studies in patients with DM having other procedures within an ERAS program or in patients with other comorbidities. In this context, the generalizability is high, as the centers cover about 40% of annual THA, TKA, and UKA in Denmark.

In summary, with the recruitment of 1007 patients with diabetes undergoing arthroplasty—of whom more than 94% had detailed perioperative assessment and treatment documented, 100% had detailed antihyperglycemic medication records, 99% had length-of-stay data registered, and the proportion with HbA1c measurements increased to 98%—the study demonstrated the feasibility of a prospective, multicenter observational study within a multicenter clinical ERAS framework [15]. This type of study may be applied to other patient groups and surgical procedures within a prospective multicenter setup. Thus, it provides relevant baseline data before deciding on large interventional randomized clinical trials [14].

Authors' contributions

Contributed to study design and devised the project: LMI, CCJ, SM, HK. Contributed to conception and design, and acquired data: MLL, CV, TJ, MRA, MJB, SO, TBH, KG, HK. Drafted the article: LMI, CCJ, SM, HK. Revised the article critically for important intellectual content: MLL, CV, TJ, MRA, MJB, SO, TBH, KG, HK. Gave final approval of the version to be published: All authors mentioned. All authors meet the ICMJE criteria for authorship and agree to be accountable for the integrity and veracity of this study and the data collected and analyzed thereafter.

Funding

Open access funding provided by Copenhagen University NOVO NORDISK Foundation, grant number NNF21SA0073760, given to the Center for Fast-Track Hip & Knee Replacement, managed by Professor Henrik Kehlet, Rigshospitalet, and Thomas Jakobsen, Aalborg Hospital. PhD student Luma Mahmoud Issa is remunerated by a grant from the NOVO NORDISK Foundation and has no financial benefit from the study.

Data availability
Data can be obtained from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Permission to collect, store, and process data was approved by the Region of Southern Denmark (Journal No 22/39454), and the study is registered on ClinicalTrials.gov (NCT05613439) by Christoffer Jørgensen on January 9th, 2022, 9 months prior to patient enrollment. According to the Danish National Ethics Committee, the study did not need approval by the Ethics Committee, as it was a non-interventional observational study. All patients provided written informed consent regarding the completion of questionnaires and data extraction from medical records.

Competing interests
SM: Advisory boards: AstraZeneca; Boehringer Ingelheim; Intarcia Therapeutics; Novo Nordisk; Sanofi, Abbott Lab, Bayer, Amgen. Lecture fees: AstraZeneca; Novo Nordisk, MSD. Research Grant Recipient: Novo Nordisk; Novo Nordisk foundation, Boehringer Ingelheim. Support for attending meetings and/or travel: Novo Nordisk, Boehringer-Ingelheim.
CV received travel expenses from Stryker paid to the institution with no relevance to the present study.
CCJ received travel expenses and lecture fees from Pharmacosmos with no relevance to the present study.
The other authors declare no conflict of interest.

Author details
[1]Department of Anaesthesia and Intensive Care, Hvidovre University Hospital, Kettegård Alle 30, Hvidovre 2650, Denmark. [2]Center for Fast-Track Hip and Knee Replacement, Denmark, Denmark. [3]Department of Anaesthesia, Hospital of Northern Zealand, Hillerød, Denmark. [4]The Department of Endocrinology, Hvidovre University Hospital, Hvidovre, Denmark. [5]Department of Orthopaedic Surgery and Traumatology, Odense University Hospital and Svendborg, Svendborg, Denmark. [6]Department of Orthopaedic Surgery, Lillebaelt Hospital—Vejle, Vejle, Denmark. [7]Department of Orthopaedic Surgery, Aalborg University Hospital, Aalborg, Denmark. [8]Department of Orthopaedic Surgery, Copenhagen University Hospital, Gentofte, Denmark. [9]Department of Orthopaedic Surgery, Næstved, Slagelse and Ringsted Hospitals, Næstved, Denmark. [10]Department of Orthopaedic Surgery and Traumatology, Copenhagen University Hospital, Copenhagen, Denmark. [11]Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark. [12]University Clinic for Hand, Hip and Knee Surgery, Hospital Unit West Jutland and Aarhus University, Aarhus, Denmark. [13]Department of Orthopaedic Surgery, Hvidovre University Hospital, Hvidovre, Denmark. [14]Section of Surgical Pathophysiology, Copenhagen University Hospital, Copenhagen, Denmark.

Received: 29 October 2024 Accepted: 28 November 2025
Published online: 13 December 2025

References

1. Buggy DJ, Nolan R, Coburn M, Columb M, Hermanides J, Hollman MW, et al. Protocol for a prospective, international cohort study on the management and outcomes of perioperative care among European diabetic patients (MOPED). BMJ Open. 2021;11:e044394.
2. Drayton DJ, Birch RJ, D'Souza-Ferrer C, Ayres M, Howell SJ, Ajjan RA. Diabetes mellitus and perioperative outcomes: a scoping review of the literature. Br J Anaesth. 2022;128:817–28.
3. Huang L, Petersen RH, Kehlet H. Postoperative outcomes in patients with diabetes after enhanced recovery thoracoscopic lobectomy. Surg Endosc. 2024;38:4207–14.
4. Gysling S, Lewis-Lloyd CA, Lobo DN, Crooks CJ, Humes DJ. The effect of diabetes mellitus on perioperative outcomes after colorectal resection: a national cohort study. Br J Anaesth. 2024;133:67–76.
5. Ortved M, Petersen PB, Jørgensen CC, Kehlet H. Postoperative morbidity and mortality in diabetic patients after fast-track hip and knee arthroplasty: a prospective follow-up cohort of 36,762 procedures. Anesth Analg. 2021;133:115–22.
6. Crowley K, Scanaill PO, Hermanides J, Buggy DJ. Current practice in the perioperative management of patients with diabetes mellitus: a narrative review. Br J Anaesth. 2023;131:242–52.
7. Madsbad S, Wiberg M, Issa LM, Schmidt S, Kehlet H. Challenges for perioperative glycaemic control in patients with diabetes. Ugeskr Laeger. 2022;184:V05220321.
8. Kehlet H. Enhanced postoperative recovery: good from afar, but far from good? Anaesthesia. 2020;75 Suppl 1:e54–61.
9. Yang DJ, Zhang S, He WL, Chen HY, Cai SR, Chen CQ, et al. Fast track surgery accelerates the recovery of postoperative insulin sensitivity. Chin Med J (Engl). 2012;125:3261–5.
10. Zhao G, Cao S, Cui J. Fast-track surgery improves postoperative clinical recovery and reduces postoperative insulin resistance after esophagectomy for esophageal cancer. Support Care Cancer. 2014;22:351–8.
11. Jorgensen CC, Madsbad S, Kehlet H. Postoperative morbidity and mortality in type-2 diabetics after fast-track primary total hip and knee arthroplasty. Anesth Analg. 2015;120:230–8.
12. Jones IA, LoBasso MA, Wier J, Gettleman BS, Richardson MK, Ratto CE, et al. Perioperative dexamethasone in diabetic patients: a systematic review and meta-analysis of randomized, placebo-controlled trials. Anesth Analg. 2024;139:479–89.
13. Shang Z, Jiang Y, Fang P, Zhu W, Guo J, Li L, et al. The association of preoperative diabetes with postoperative delirium in older patients undergoing major orthopedic surgery: a prospective matched cohort study. Anesth Analg. 2024;138:1031–42.
14. Kehlet H, Lobo D. Exploring the need for reconsideration of trial design in perioperative outcomes research: a narrative review. EClinicalMedicine. 2024;70:102510.
15. Issa LM, Kehlet H, Madsbad S, Lindberg-Larsen M, Varnum C, Jakobsen T, et al. Protocol for a prospective multicentre cohort study to address the question whether diabetes and its management is still a risk factor in fast-track joint arthroplasty. BMJ Open. 2024;14:e080232.
16. Danielsen O, Varnum C, Jensen CB, Jakobsen T, Andersen MR, Bieder MJ, et al. Implementation of outpatient hip and knee arthroplasty in a multicenter public healthcare setting. Acta Orthop. 2024;95:219–24.
17. Lindberg-Larsen M, Varnum C, Jakobsen T, Andersen MR, Sperling K, Overgaard S, et al. Study protocol for discharge on day of surgery after hip and knee arthroplasty from the Center for Fast-track Hip and Knee Replacement. Acta Orthop. 2023;94:121–7.
18. Lancaster GA, Thabane L. Guidelines for reporting non-randomised pilot and feasibility studies. Pilot Feasibility Stud. 2019;5:114.
19. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42:377–81.
20. Sauro KM, Smith C, Ibadin S, Thomas A, Ganshorn H, Bakunda L, et al. Enhanced recovery after surgery guidelines and hospital length of stay, readmission, complications, and mortality: a meta-analysis of randomized clinical trials. JAMA Netw Open. 2024;7:e2417310.

Publisher's Note