UNIVERSITÄT AUGSBURG
Universitätsbibliothek

OPEN ACCESS
OPUS AUGSBURG

Heidelberg Perioperative Deep Data Study (HeiPoDD): study protocol for a prospective cohort study for prediction of complications after high-risk non-cardiac surgery in a German university hospital

Mona Jung-König, Hans Thomas Hölzer, Solveig Tenckhoff, Sachin Kumar, Melanie Etheredge, Dominik Schaack, Tobias Hölle, Laura Christine Schuster, Christian Nusshag, Mathias Rath, Christian Uhl, Frank Pianka, Christoph W. Michalski, Markus Hohenfellner, Rawa Arif, Matthias Karck, Dittmar Böckler, Pascal Probst, Markus Diener, Markus A. Weigand, Martin Dugas, Christian Niklas, Manuel Feißt, Rosa Klotz, Jan Larmann

Angaben zur Veröffentlichung / Publication details:

Jung-König, Mona, Hans Thomas Hölzer, Solveig Tenckhoff, Sachin Kumar, Melanie Etheredge, Dominik Schaack, Tobias Hölle, et al. 2025. "Heidelberg Perioperative Deep Data Study (HeiPoDD): study protocol for a prospective cohort study for prediction of complications after high-risk non-cardiac surgery in a German university hospital." *BMJ Open* 15 (9): e098590. https://doi.org/10.1136/bmjopen-2024-098590.

Nutzungsbedingungen / Terms of use:

CC BY-NC 4.0

Dieses Dokument wird unter folgenden Bedingungen zur Verfügung gestellt: / This document is made available under these conditions:
CC-BY-NC 4.0: Creative Commons: Namensnennung - Nicht kommerziell
Weitere Informationen finden Sie unter: / For more information see:
https://creativecommons.org/licenses/by-nc/4.0/deed.de

BMJ Open

Heidelberg Perioperative Deep Data Study (HeiPoDD): study protocol for a prospective cohort study for prediction of complications after high-risk non-cardiac surgery in a German university hospital

Mona Jung-König,[1] Hans Thomas Hölzer ,[1] Solveig Tenckhoff,[2] Sachin Kumar,[1,3] Melanie Etheredge,[1,3] Dominik Schaack,[1] Tobias Hölle,[1] Laura Christine Schuster,[1] Christian Nusshag,[4] Mathias Rath,[5] Christian Uhl,[6,7] Frank Pianka,[8,9] Christoph W Michalski,[9] Markus Hohenfellner,[5] Rawa Arif,[10] Matthias Karck,[10] Dittmar Böckler,[6] Pascal Probst ,[8,11] Markus Diener,[8,12] Markus A Weigand,[1] Martin Dugas ,[13] Christian Niklas,[13] Manuel Feißt,[14] Rosa Klotz,[2,8] Jan Larmann [1,3]

To cite: Jung-König M, Hölzer HT, Tenckhoff S, *et al*. Heidelberg Perioperative Deep Data Study (HeiPoDD): study protocol for a prospective cohort study for prediction of complications after high-risk non-cardiac surgery in a German university hospital. *BMJ Open* 2025;**15**:e098590. doi:10.1136/bmjopen-2024-098590

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2024-098590).

Received 28 December 2024
Accepted 07 August 2025

Linked

► http://dx.doi.org/10.1136/bmjopen-2024-098589

Check for updates

© Author(s) (or their employer(s)) 2025. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ Group.

For numbered affiliations see end of article.

Correspondence to
Jan Larmann;
an-direktion@ukaachen.de

ABSTRACT

Introduction Perioperative adverse events increase morbidity and mortality. The rate and severity of complications and the risk for subsequent mortality are increased after high-risk procedures and in elevated-risk patients. Over the past decades, a multitude of prognostic studies identified perioperative risk factors at the population level. However, to allow for the advancement of precision surgery strategies, improved risk prediction on the individual patient level is warranted. Comprehensive, consecutive, multisource, structured, high-quality patient-related and procedure-related data sets, together with thorough follow-up and combined with state-of-the-art machine-learning analyses, are needed to facilitate precise prediction of perioperative complications. Therefore, we designed and currently conduct the Heidelberg Perioperative Deep Data study (HeiPoDD). Here, we report the rationale and design of the HeiPoDD study.

Methods and analysis HeiPoDD is a prospective, single-centre, exploratory cohort study aiming to build up a large-scale deep-data base and corresponding biomaterial collection. 1040 adult patients planned for elective high-risk, non-cardiac surgery for any indication at Heidelberg University Hospital, Germany will be included. The obtained study-specific data set includes clinical data, lab values, genome- and proteome analysis as well as plasma, serum and peripheral blood mononuclear cells (PBMC) collected before and at days 1, 3 and 7 postsurgery. Urine samples are collected before and at day 1 postsurgery. Structured follow-up for perioperative complications such as redo-surgery, length of intensive care stay or length of hospital stay is conducted at days 30, 90 and 1 year postsurgery and for disease progression and survival after 3 and 5 years postsurgery. All study data will be transferred to the HeiPoDD registry to allow merging with all available routine clinical data from the hospital information system including imaging studies as well as haemodynamic and respiratory biosignals. Biomaterials will be stored in the HeiPoDD biomaterial bank to allow further analyses.

Ethics and dissemination The trial protocol and amendments were approved by the ethics committee of the University of Heidelberg (S-758/2021). The protocol is registered with the German Clinical Trial Register (DRKS00024625). Participating patients' data will be recorded only in pseudonymised form. After completion of the study, data collected during the study will be kept on file for up to 30 years. Biomedical samples collected during the study and entered into the biobank will be held for the same amount of time. The findings will be disseminated in peer-reviewed academic journals.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The Heidelberg Perioperative Deep Data study is one of the first prospective studies to generate a comprehensive, consecutive, multisource, structured, perioperative data set with a 5 year follow-up.
⇒ Broad inclusion criteria will allow for a representative study collective.
⇒ The generalisability of findings will be limited by the monocentric design of the study.

INTRODUCTION

Worldwide, the number of surgeries is increasing, more than 300 million surgical procedures are performed each year.[1] Likewise, following demographic change and the development of improved therapeutic

BMJ Open: first published as 10.1136/bmjopen-2024-098590 on 10 September 2025. Downloaded from http://bmjopen.bmj.com/ on September 10, 2026 at UB Augsburg . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

concepts, the rate of older and multimorbid patients undergoing surgery increases. Consequently, not only is the number of surgeries expanding, but also the number of complications. In a large-scale prospective cohort study, 16.8% of the over 44 000 patients undergoing elective surgery developed a relevant complication, and complications were associated with a fivefold increase in mortality.[2]

Patients undergoing high-risk procedures and individuals with patient-related risk factors such as cardiovascular disease or chronic kidney disease are prone to perioperative complications and subsequent morbidity and mortality.[3 4] Perioperative immune dysfunction drives cardiovascular disease, and strategies tailored for immunomodulation might prevent complications.[5–7] Understanding underlying mechanisms on the cellular and molecular level and the development of concepts for individual prediction of surgery-associated complications will foster precision surgery.

Precision surgery concepts aim to allow the best surgical outcome possible and to minimise complications at the same time. Precise prediction of complications is a prerequisite to tailor therapy and prophylactic strategies to the individual patient. Therefore, identifying patients at risk and a better understanding of complications helps to improve patient outcomes.

Over the past decades, a multitude of prognostic studies identified perioperative risk factors on the population level.[6 8 9] However, even the combination of several prognostic factors has little benefit for predicting complications in individual patients undergoing a specific procedure for a given disease.

To allow the advancement of precision surgery strategies, improved risk prediction on the individual patient level is warranted. Comprehensive, consecutive, multisource, structured, high-quality patient-related and procedure-related data sets, together with thorough follow-up and combined with state-of-the-art machine-learning analyses, are needed to facilitate precise prediction of perioperative complications.

The increasing availability of cost-effective memory space and distributed high-performance computing capacity has led to the rapid development of machine learning (ML) algorithms. In the last few years, ML algorithms have proved to solve prediction and classification tasks in medicine, previously known to require intelligent assessment of available data.[10–12] The perioperative setting is ideal for ML methods, because of a highly parametric and in many places automated patient data collection. Various studies have been published using ML to predict perioperative complications in retrospective surgical cohorts.

Regularly, ML algorithms have been shown to even outperform conventional models of risk prediction in this setting.[13] But meaningful and reliable predictions are only possible if specific perioperative events and outcomes are recorded in a structured, uniform way.[14] This will especially improve the feasibility of ML methods that

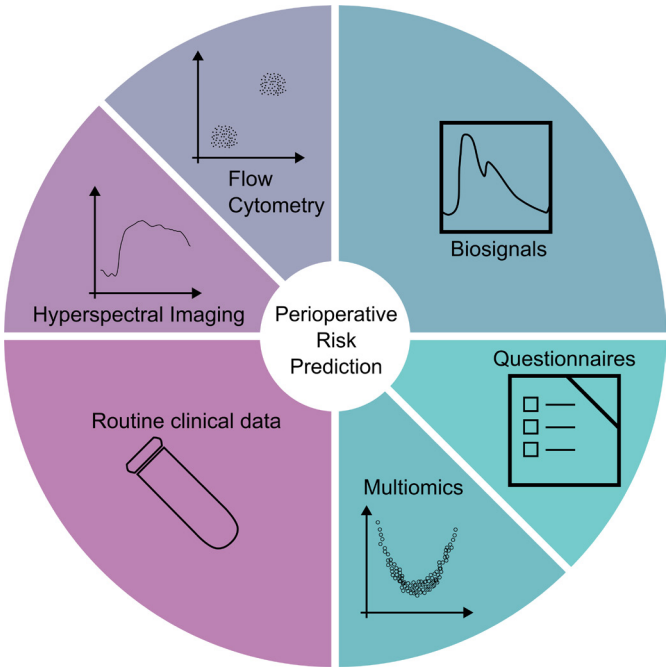


Figure 1 In the prospective HeiPoDD study, data such as hyperspectral images and biomaterials—including plasma and urine samples—will be collected from 1040 patients over the course of up to 13 visits. These data will be transferred to the HeiPoDD registry and biomaterial bank, where they will be integrated with routine clinical data and monitored biosignals. HeiPoDD, Heidelberg Perioperative Deep Data

fall under the category of supervised learning. Previous studies using ML algorithms handled mostly retrospective data sets. A methodological consensus for good scientific documentation of studies involving artificial intelligence (AI) in medicine was recently published by the CONSORT (CONsolidated Standards Of Reporting Trials) AI initiative.[15] This stems from the identified need for more prospectively planned studies in medical AI, leading to improved data quality. Due to the novelty of this guidance, so far only a few studies on ML in medicine employed these high-quality standards.

Therefore, we are conducting the prospective Heidelberg Perioperative Deep Data (HeiPoDD) study.

The combination of a highly detailed data set, supplemented by longitudinal biological samples, will provide unprecedented opportunities for the identification of novel biomarkers, the opportunity to build precise risk prediction models and to support precision surgery concepts for improving outcomes and reducing complications (figure 1).

METHODS AND ANALYSIS

Objective

With the goal to comprehensively characterise surgical patients to identify novel biomarkers associated with complications after major non-cardiac surgery and explore postoperative outcome measures using

BMJ Open: first published as 10.1136/bmjopen-2024-098590 on 10 September 2025. Downloaded from http://bmjopen.bmj.com/ on September 10, 2026 at UB Augsburg . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

data-driven, personalised risk prediction, we currently conduct the HeiPoDD study.

Study design

The HeiPoDD study is a prospective, non-interventional, single-centre, exploratory, observational cohort study. The first patient was included on 17 January 2022. It is planned to include the last patient on 31 December 2025.

Study population

The study is being conducted in the surgical centre at the University Hospital Heidelberg, Heidelberg, Germany, where patients from the department of general, visceral and transplantation surgery, the department of vascular surgery and the department of urology are operated on.

All patients undergoing elective high-risk, non-cardiac surgery for any indication, as defined by the European Society of Anaesthesiology and Intensive Care (ESAIC), are eligible.[16] This includes oesophagectomy (partial) gastrectomy, major colon surgery, repair of perforated bowel, duodeno-pancreatic surgery, liver resection, bile duct surgery, adrenal resection, pneumonectomy, pulmonary or liver transplant, nephrectomy for polycystic kidney disease, total cystectomy, paraaortic lymphadenectomy, aortic and major vascular surgery, open lower limb revascularisation or amputation or thromboembolectomy. Additional inclusion criteria are as follows: age of 18 years or older, ability of the subject to understand character and individual consequences of the study, written informed consent and inclusion in the HeiPoDD registry. Exclusion criteria are expected lack of compliance or language barriers, Jehovah's Witnesses and ASA classification ≥5. All patients planned for high-risk procedures will be screened for eligibility. Screening is conducted prior to the day of surgery. Because the number of eligible patients occasionally exceeds the available human resources, the maximum number of patients to be recruited on a given day is specified in advance. Subsequently, all eligible patients will be automatically listed in a random order using a digital randomisation function. Screening will follow the order on this list until the maximum number of patients to be included on this day has been reached or until all patients on the list have been screened. Participation is voluntary. Patients are free to stop their study participation at any time and ask for the removal of data and biomaterials without disadvantages and without giving reasons for their decision.

Premature closure or extension of the study

The study may be prematurely closed by the principal investigator if the patient's enrolment is unsatisfactory concerning quality and/or quantity, data recording is severely inaccurate and/or incomplete and external evidence demanding a termination. The time of recruitment may be adapted after consultation if the required number of patients has not been recruited, or if a higher number of patients is needed to implement and validate ML algorithms.

Study-related measures

The study is designed for identification of risk factors and initial development, refinement and/or validation of algorithms and prediction models on a comprehensive data set of 1040 patients. Study data and biomaterials will be transferred into the HeiPoDD registry and biomaterial bank. This database will contain clinical routine data, such as demographic data, laboratory results, medical history, imaging data and intraoperative haemodynamic monitoring signals stored in a highly structured form, which will be supplemented by study-specific anamnestic data, ECGs, blood samples and outcome parameters collected as part of the clinical study.[17] As specified in several amendments to the study protocol, the data set is supplemented by food frequency, long COVID questionnaires and hyperspectral imaging measurements for a subset of patients. In addition, 1, 3 and 5 year follow-up visits, including quality of life (SF-12) and long-time outcome questionnaires, will be performed. Blood will be collected during four visits to allow for serial analysis and diagnosis of complications, such as perioperative myocardial infarction/injury or acute perioperative kidney injury/changes in kidney function. In addition, blood samples will be collected for genotyping, plasma proteome analysis and flow-cytometry-based immunophenotyping (see table 1).

Outcome parameters

The outcome parameters include surgery-specific and anaesthesiologic outcome parameters. Outcome measures include short-term endpoints, for example, complications, time to functional recovery and quality of life (measured by SF-12). A 5 year follow-up period will allow the evaluation of long-term endpoints such as 1, 3 and 5 year survival and tumour recurrence (see online supplemental file 1).

Participant timeline

During the study, up to 13 visits will be conducted (see tables 2 and 3). After the preoperative screening visit (V1) and the surgery itself (V2), inpatient follow-up visits on postoperative days 1, 3, 7 and 14 (V3–V6) are planned for evaluation of predefined endpoints. Visit 7 is on the day of discharge. If discharge occurs before visits 4, 5 or 6, the respective postoperative visits can be omitted. In addition, 30 and 90 days after surgery, telephone or inpatient follow-up visits (V8 and V9) will be performed to evaluate postoperative outcomes. 1, 3 and 5 years postoperatively, telephone long-term follow-up will be performed (V10–V12). The participation of the patients is concluded by an end-of-study participation visit (V13). The end-of-study visit contains information about regular or non-regular termination of the study participation. In the case of

BMJ Open: first published as 10.1136/bmjopen-2024-098590 on 10 September 2025. Downloaded from http://bmjopen.bmj.com/ on September 10, 2026 at UB Augsburg . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 1 Study-specific laboratory results, blood and urine samples and material for biobanking

Time	Analysis	Biobank
Before surgery	hs-cTNT, NT-proBNP, creatinine, LDH, transferrin, ferritin, transferrin saturation, differential blood count, proteome, immunophenotyping, fibrinogen, viscoelastometry	EDTA, serum gel, hep plasma, urine, RNA tube, PBMC
POD 1	hs-cTNT, NT-proBNP, creatinine, LDH, differential blood count, proteome, immunophenotyping, viscoelastometry, fibrinogen	EDTA, serum gel, hep plasma, urine, RNA tube, PBMC
POD 3	hs-cTNT, NT-proBNP, creatinine, LDH, differential blood count, proteome, immunophenotyping	EDTA, serum gel, hep plasma, RNA tube, PBMC
POD 7	hs-cTNT, NT-proBNP, creatinine, LDH, transferrin, ferritin, transferrin saturation, differential blood count, proteome, immunophenotyping	EDTA, PBMC

EDTA, Ethylenediaminetetraacetic acid; hep, Heparin; hs-cTNT, High-Sensitivity Cardiac Troponin T; LDH, Lactate dehydrogenase; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; PBMC, Peripheral blood mononuclear cell; PBMC, Peripheral blood mononuclear cell; POD, Postoperative day; RNA, Ribonucleic acid.

premature study termination, the questions of visit 13 will be filled out, which include the documentation of the date of study termination as well as the reason for study termination.

Safety aspects

The study endpoints include all necessary safety endpoints. No additional safety analysis will be performed in this study. For clinical studies according to the Medical Association's professional code (Berufsordnung der Landesärztekammer Baden-Württemberg) section 15, no specific serious adverse event management is required in Germany.

Sample size calculation

Due to the exploratory character of the study, no formal sample size calculation has been conducted. All patients undergoing elective high-risk, non-cardiac surgery at the Heidelberg University Hospital surgical centre are screened as of January 2022. It is planned to include 1040 patients in the study, so that at least 1000 analysable index operations take place. Until short-term follow-up at day 90 postsurgery, we expect 5% of patients to drop out, and until long-term follow-up, we expect a drop-out rate of 10%. The resulting sample size is deemed sufficient to adequately perform the analyses and build robust models for a variety of endpoints.

Table 2 Overview of the short-term study-specific visits

	V1	V2	V3	V4	V5	V6	V7	V8
	Before surgery	Day of surgery	POD 1	POD 3	POD 7	POD 14	Day of discharge	POD 30
Visit	Inpatient							Inpatient/ per telephone
Eligibility criteria	X							
Informed consent	X							
Baseline demographic and clinical data	X							
QoL questionnaires	X							X
Blood sample	X		X	X	X		X	
ECG	X			X	X		X	
Intraoperative endpoints		X						
Pain/nausea	X		X	X			X	X
Short-term endpoints			X	X	X	X	X	X

ECG, Electrocardiogram ; POD, Postoperative day; QoL, Quality of life; V, Visit.

BMJ Open: first published as 10.1136/bmjopen-2024-098590 on 10 September 2025. Downloaded from http://bmjopen.bmj.com/ on September 10, 2026 at UB Augsburg . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 3 Overview of the long-term study-specific visits

Visit	V9 POD 90 Inpatient/per telephone	V10 1 year Per telephone	V11 3 years	V12 5 years	V13 End of study
QoL questionnaires	X	X	X	X	
Pain/nausea	X	X	X	X	
Long-term endpoints	X	X	X	X	X

POD, Postoperative day; QoL, Quality of life; V, Visit.

Statistical analysis

The study cohort as well as the study endpoints will be described by tabulation of the measures of the empirical distributions. According to the scale level of the variables, means, SDs, medians, first and third quartiles, minimum and maximum (for continuous variables) or absolute and relative frequencies will be reported (for categorical variables), respectively.

Furthermore, endpoint-specific prediction models will be built. Thereby, logistic regression models as well as ML algorithms, for example, neural networks, tree-based models and elastic nets, will be used and their results will be compared with appropriate statistical measures (eg, area under the curve of the receiver operating characteristic curve, accuracy, kappa statistics). In addition, these analyses will comprise variable selection procedures to identify the most important prediction factors. Appropriate adjustments for multiple comparisons will be made. All analyses will be performed using the statistical software R V.>4.00.0 as well as with Python V.>3.80.0.

Data collection and data management

All protocol-required information collected during the study is entered by the investigator or designated representative in the electronic case report form (eCRF). The study personnel will complete the eCRF pages as soon as possible after the information is collected. Any missing entries will be completed immediately after the final examination. All changes to data are logged with a computerised timestamp in an audit trail. An explanation will be given for all missing data. To assure a safe and secure environment for data acquired, data transmission is encrypted with secure socket layer technology. Completeness, validity and plausibility of data will be checked at the time of data entry (edit-checks) using validating programmes. If no further corrections are to be made in the data base, eCRF data will be locked. All data management procedures will be conducted according to written, defined standard operating procedures. At the end of the study, the data will be transformed into different data formats for archiving and to ensure that it can be reused. All study data will be included in the HeiPoDD registry.[17]

Patient and public involvement

Patients and public were not involved in the study design process.

ETHICS AND DISSEMINATION

Study registration, ethics and consent

This trial protocol was approved by the ethics committee of the University of Heidelberg (Ethikkommission Medizinische Fakultät Heidelberg, S-758/2021, 4 November 2021). It was registered at the German clinical trial register (DRKS00024625, 7 December 2021) before inclusion of the first patient. The ethics committee will be informed of all subsequent protocol amendments to determine whether formal approval needs to be sought. So far, the following changes in six amendments have been approved by the ethics committee: adding an end-of-study visit, adding questions about post-COVID symptoms, adding questions about pain in visits 7, 8, 9, 10, 11 and 12, expanding the study from 640 to 1040 patients, adjusting the timeframe of the study and of the visits, adapting the number and type of blood-collection tubes, adding questions about dietary behaviour, dyspnoea and ascites, changes in personnel, adding questions about therapy adherence, adding hyperspectral, fibrinogen, thromboelastic measurements and removal of choice options for endpoints that were not applicable and for drugs that were not used. The study is designed according to the Medical Association's professional code (Berufsordnung der Landesärztekammer Baden-Württemberg) section 15 (non-AMG/non-MPG trials). The principal investigator will ensure that the implementation will take place in the context of GCP (ICH E6) and in accordance with the Declaration of Helsinki (in its current version). All patients will be informed verbally and in writing. Study aims, consequences and possible risks and benefits will be exposed in detail. It is the responsibility of the study physician to emphasise that participation is voluntary and that the patient is allowed to withdraw further study participation at any time without giving reasons. This will not prejudice the patient's subsequent care. In this case, patients will be asked whether the data recorded up to that date may be used in the analysis of the trial or if it should be discarded. The written informed consent form will be signed and personally dated by the patient

BMJ Open: first published as 10.1136/bmjopen-2024-098590 on 10 September 2025. Downloaded from http://bmjopen.bmj.com/ on September 10, 2026 at UB Augsburg . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

according to GCP guidelines after sufficient time to decide on participation.

Confidentiality

Patients will be informed as to the strict confidentiality of their data, but that their medical records may be reviewed for study purposes by authorised individuals other than their treating physician. It is the responsibility of the investigator to maintain patients' confidentiality. During the study, patients will be identified solely using their individual identification codes. Study-specific documents will be stored in accordance with local data protection law and ICH-GCP guidelines and will be handled in strictest confidence. For the protection of these data, organisational procedures are implemented to prevent the distribution of data to unauthorised persons. The study centre will maintain a personal subject identification list (screening numbers with the corresponding subject names) to enable records to be identified. The patient data will be transferred in a pseudonymised form by the study centre. Names and all confidential data of participating patients will be handled in line with the obligations of medical secrecy, the European General Data Protection Regulation (Datenschutzgrundverordnung, DSGVO), the Federal Data Protection Act (Bundesdatenschutzgesetz) and the state Data Protection Act (Landesdatenschutzgesetz). Participating patients' data will be recorded only in pseudonymised form. Third parties have no access to original documents. After completion of the study, data collected during the study will be kept on file for up to 30 years. Biomedical samples collected during the study and entered into the biobank will be held for the same amount of time (up to 30 years) as the study data.

Access to data

Original data access will be restricted to the electronic data base manager, study project manager, study nurses, scientific physicians and medical doctoral students for study visits.

Risk–benefit assessment

The study will not interfere with any aspects of clinical care. There is a minimal additional risk of haematoma, infection or neuronal damage when collecting blood samples, for which patients give informed consent. Furthermore, the risks are limited to data protection. There is no direct benefit for participating patients. However, this study aims to improve the understanding and the individual predictability of complications after elective high-risk non-cardiac surgery. In the future, this knowledge might allow for the prediction of the individual risk of complications and could serve as the base in the prevention of these risks, for example, through intensified care, modified treatment or earlier diagnosis and therapy of complications that occur, nevertheless. Therefore, the study will contribute to the gain in scientific knowledge and future patients will likely benefit from the results of the current study.

Dissemination policy

After completion of the data collection, all data and stored bio materials will be available for further analyses in the HeiPoDD registry and biomaterial bank. Data may be made available to third parties, like universities or research institutes, on request for research purposes only through access to the HeiPoDD registry.[17] The data will be analysed and results published in a peer-reviewed journal. This protocol publication follows the STROBE (strengthening the reporting of observational studies in epidemiology) guidelines.[18] The full study protocol will be available on request.

DISCUSSION

As the HeiPoDD study is a prospective study that collects data in a structured manner, a high data quality will be aimed for. The study-specific measurements, such as ECGs and additional blood samples, in combination with routine clinical data, generate a sufficient data resolution for complex ML algorithms. Current scoring systems for perioperative complications and mortality are often not sufficient and often based on retrospective data. ML algorithms provide possibilities to create more specific scoring systems and to identify risk factors for specific outcomes. These advantages will support clinical decision-making and therefore improve patient outcomes.

One limitation of the HeiPoDD study is the generalisability of the results, as the study is monocentric. Furthermore, due to the broad inclusion criteria and due to the number of patients included, the study will not have a sufficiently high number of cases for an accurate prediction of rare complications. Due to the study design, no blinding will be done; therefore, no causal relations can be described. The data base contains only a few socioeconomic information. Therefore, to conduct analyses with respect to social aspects influencing outcome, our data need to be combined with other specialised data bases.

Within the HeiPoDD study, it will be possible to identify biomarkers for a wide variety of diseases or complications. The data of the HeiPoDD study will be included in the HeiPoDD registry and biomaterial bank. Based on the analysis of the HeiPoDD data, further studies will follow to investigate risk prediction models and new biomarkers.

Author affiliations
[1]Department of Anesthesiology, Heidelberg University, Medical Faculty Heidelberg, Heidelberg, Germany
[2]The Study Center of the German Surgical Society, Heidelberg University, Heidelberg, Germany
[3]Department of Anaesthesiology, Medical Faculty, RWTH Aachen University, Aachen, Germany
[4]Department of Nephrology, Heidelberg University, Medical Faculty Heidelberg, Heidelberg, Germany
[5]Department of Urology, Heidelberg University, Medical Faculty Heidelberg, Heidelberg, Germany
[6]Department of Vascular and Endovascular Surgery, Heidelberg University, Medical Faculty Heidelberg, Heidelberg, Germany
[7]Department of Vascular Surgery, Medical Faculty, RWTH Aachen University, Aachen, Germany

BMJ Open: first published as 10.1136/bmjopen-2024-098590 on 10 September 2025. Downloaded from http://bmjopen.bmj.com/ on September 10, 2026 at UB Augsburg . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

[8]Department of General, Visceral and Transplantation Surgery, Heidelberg University, Medical Faculty Heidelberg, Heidelberg, Germany
[9]Department of General, Visceral and Transplantation Surgery, Heidelberg University, Clinical Study Center, Heidelberg, Germany
[10]Department of Cardiac Surgery, Heidelberg University, Medical Faculty Heidelberg, Heidelberg, Germany
[11]Department of Surgery, Cantonal Hospital Thurgau, Frauenfeld, Switzerland
[12]Department of General, Visceral and Thoracic Surgery, Klinikum Nuernberg, Germany
[13]Heidelberg University, Medical Faculty Heidelberg, Institute of Medical Informatics, Heidelberg, Germany
[14]Institute of Medical Biometry, Heidelberg University, Heidelberg, Germany

Acknowledgements The authors thank the whole Heidelberg Perioperative Deep Data (HeiPoDD) study team and the surgical centercentrecentre team for their cooperation to make this study possible. For the publication fee we acknowledge financial support by Heidelberg University.

Contributors MJ-K, HTH, ST, SK, ME, DS, TH, LCK, CNu, MR, CU, FP, CWM, MH, RA, MK, DB, PP, MDi, MAW, Mdu, CNi, MF, RK and JL are responsible for the study design, definition of endpoints and preparation of the protocol. JL is the guarantor. MF is the responsible biometrician and takes care of the statistical design. MJ-K, CNi, HTH and JL wrote the first draft of the protocol publication. Furthermore, ST, SK, ME, DS, TH, LCK, CNu, MR, CU, FP, CWM, MH, RA, MK, DB, PP, MDi, MAW, Mdu, MF and RK revised and all approved the final manuscript critically. The authorship criteria of the *International Committee of Medical Journal Editors* (*ICMJE*) will be applied.

Funding HeiPoDD was funded by the Ministerium für Wissenschaft, Forschung und Kunst Baden-Württemberg (42-5400/70/1) and supported through state funds approved by the State Parliament of Baden-Württemberg for the Innovation Campus Health + Life Science alliance Heidelberg Mannheim (32-7531-25/5/18) and departmental funds from the Departments of Anaesthesiology and General, Visceral and Transplant Surgery, Heidelberg University Hospital, Heidelberg Germany. All aspects of the study will be conducted independently from any funding source, including study design and conduct, analysis and interpretation of data as well as submission of the report for publication.

Competing interests Yes, there are competing interests for one or more authors. Dr Larmann reported grants from Philips and personal fees from Philips not related to the submitted work. Dr Hölzer reported payment for presentations to the institution from Philips not related to the submitted work and grants from the Ministerium für Wissenschaft, Forschung und Kunst BadenWürttemberg. All other authors have no completing interest to declare.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID iDs
Hans Thomas Hölzer http://orcid.org/0000-0003-2414-2727
Pascal Probst http://orcid.org/0000-0002-0895-4015
Martin Dugas http://orcid.org/0000-0001-9740-0788
Jan Larmann http://orcid.org/0000-0003-3365-4572

REFERENCES

1 Weiser TG, Haynes AB, Molina G, *et al*. Estimate of the global volume of surgery in 2012: an assessment supporting improved health outcomes. *Lancet* 2015;385 Suppl 2:S11.
2 ISOS-Group. Global patient outcomes after elective surgery: prospective cohort study in 27 low-, middle- and high-income countries. *Br J Anaesth* 2016;117:601–9.
3 Handke J, Scholz AS, Gillmann H-J, *et al*. Elevated presepsin is associated with perioperative major adverse cardiovascular and cerebrovascular complications in elevated-risk patients undergoing noncardiac surgery: the leukocytes and cardiovascular perioperative events study. *Anesth Analg* 2019;128:1344–53.
4 Liao C-C, Liu C-C, Lee Y-W, *et al*. Complications and mortality after surgery in patients with chronic kidney disease: a retrospective cohort study based on a multicenter clinical database. *J Multidiscip Healthc* 2024;17:3535–44.
5 Janssen H, Felgner L, Kummer L, *et al*. Sequential surgical procedures in vascular surgery patients are associated with perioperative adverse cardiac events. *Front Cardiovasc Med* 2020;7.
6 Scholz AS, Handke J, Gillmann H-J, *et al*. Frontline science: low regulatory T cells predict perioperative major adverse cardiovascular and cerebrovascular events after noncardiac surgery. *J Leukoc Biol* 2020;107:717–30.
7 Handke J, Kummer L, Weigand MA, *et al*. Modulation of peripheral CD4+CD25+Foxp3+ regulatory T cells ameliorates surgical stress-induced atherosclerotic plaque progression in ApoE-deficient Mice. *Front Cardiovasc Med* 2021;8:682458.
8 Lee TH, Marcantonio ER, Mangione CM, *et al*. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation* 1999;100:1043–9.
9 Gupta PK, Gupta H, Sundaram A, *et al*. Development and validation of a risk calculator for prediction of cardiac risk after surgery. *Circulation* 2011;124:381–7.
10 Komorowski M, Celi LA, Badawi O, *et al*. The artificial intelligence clinician learns optimal treatment strategies for sepsis in intensive care. *Nat Med* 2018;24:1716–20.
11 Gulshan V, Peng L, Coram M, *et al*. Development and validation of a deep learning algorithm for detection of diabetic retinopathy in retinal fundus photographs. *JAMA* 2016;316:2402–10.
12 Esteva A, Kuprel B, Novoa RA, *et al*. Dermatologist-level classification of skin cancer with deep neural networks. *Nature New Biol* 2017;542:115–8.
13 Allyn J, Allou N, Augustin P, *et al*. A comparison of a machine learning model with euroscore ii in predicting mortality after elective cardiac surgery: a decision curve analysis. *PLoS One* 2017;12.
14 Uciteli A, Neumann J, Tahar K, *et al*. Ontology-based specification, identification and analysis of perioperative risks. *J Biomed Semantics* 2017;8.
15 Liu X, Rivera SC, Moher D, *et al*. Reporting guidelines for clinical trial reports for interventions involving artificial intelligence: the CONSORT-AI Extension. *BMJ* 2020;370.
16 Kristensen SD, Knuuti J, Saraste A, *et al*. 2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur Heart J* 2014;35:2383–431.
17 Hölzer HT, Niklas C, Tenckhoff S, *et al*. Heidelberg perioperative deep data registry and biomaterial bank (HeiPoDD - Registry and Bio Bank) - study protocol for a prospective single-center registry and biobank for patients undergoing high-risk non-cardiac surgery in a German university hospital. *BMJ Open* 2025;15.
18 Elm E von, Altman DG, Egger M, *et al*. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ* 2007;335:806–8.

BMJ Open: first published as 10.1136/bmjopen-2024-098590 on 10 September 2025. Downloaded from http://bmjopen.bmj.com/ on September 10, 2026 at UB Augsburg . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.