Sustainable anaesthesia practices in **Europe** – a multicentre, prospective, observational study (SUSTAIN-EUROPE)

Study protocol
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Protocol Signature Page

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Local Principal Investigators (enter local details, as applicable)		
Name - Place	**Signature**	**Date**
I confirm that I have read and understood the protocol, acknowledge my responsibilities as Principal Investigator, and commit to conducting the study in accordance with the protocol, Good Clinical Practice (GCP), and all applicable regulatory requirements. I will ensure that any protocol deviations are appropriately documented.		

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Synopsis (Appendix 1)

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Title	Sustainable anaesthesia practices in Europe – a multicentre, prospective observational study (SUSTAIN-EUROPE)
Short Title	SUSTAIN-EUROPE
Trial Registration	NCT07252973
Protocol Version	V1.0
Background	In response to the climate crises, Societies of Anaesthesiology call for action to reduce the carbon footprint of daily clinical work. They recommend the use of regional and total intravenous anaesthesia, and for inhalational anaesthesia cases, the use of sevoflurane with minimal fresh gas flow (FGF) settings < 0.5 l min^{-1}. Surprisingly, the type of anaesthesia and ventilation settings commonly used remain largely unknown.
Objectives	SUSTAIN-EUROPE aims to describe the current anaesthesia practices in paediatric and adult patients undergoing surgery or a procedure with anaesthesia care across Europe (including inhalational and intravenous general anaesthesia, regional anaesthesia, sedation, and combinations thereof) in a large-scale, prospective, observational study. By providing information on the status-quo we seek to identify potential areas for improvement of sustainable practices that can be addressed in future studies.
Study design	This study is designed as a multicentre, prospective, observational study. At participating European departments of anaesthesiology, eligible cases will be included within a predefined study period. For each case, routine clinical data will be obtained once at a standardized time point during the procedure (5-60 minutes after skin incision or start of procedure, respectively).
Outcomes	Primary endpoint: • Type of anaesthesia (inhalational and total intravenous general anaesthesia, regional anaesthesia, sedation, combinations, monitoring only) Secondary endpoints: • Proportional use of kind of inhalational anaesthetics in inhalational anaesthesia cases • FGF used stratified by total intravenous anaesthesia (TIVA) and inhalational general anaesthesia; for inhalational cases further stratified by use of manual settings versus automated end-tidal dosing control

	• MAC (age-adjusted), expiratory fraction and vaporiser settings in inhalational anaesthesia cases • Proportion of kind of main i.v. medication used in TIVA cases • Proportion of inhalational inductions • Proportional use of inhalational agent capture and automated end-tidal dosing control • Rebreathing fraction (FGF/expired minute volume ventilation) in general anaesthesia cases • Among procedures anatomically amenable to regional anaesthesia alone, distribution of documented reasons for not using regional anaesthesia as the sole technique • Use of depth of anaesthesia monitoring, corresponding values and availability of density spectral array • MAC (age-adjusted) and depth of anaesthesia monitoring stratified by FGF rates • proportional use of antiemetics • ventilation settings in general anaesthesia cases including tidal volume kg^{-1} ideal body weight, ventilation pressures, fraction of inspired oxygen, respiratory rate, and end-tidal carbon dioxide
Inclusion & Exclusion Criteria	**Inclusion criteria:** All patients receiving any form of anaesthesia care (whether general or regional anaesthesia, monitored sedation, combinations thereof or monitoring only) from an anaesthetist at an anaesthesia workstation in participating European departments of anaesthesiology during the selected data-collection period. **Exclusion criteria**: Patients (or legal guardians) who decline consent and patients for whom valid informed consent cannot be obtained due to language barriers or other factors preventing adequate information and understanding.
Number of Participants	At least 8000 cases.
Duration	1 week (=5 consecutive working days) for each participating centre; 1 year for the entire study; patient-level data collection at a single time point 5-60 minutes after skin incision or start of procedure, respectively.
Centres	All departments of anaesthesiology from European hospitals are invited to participate.
Statistical Considerations	Descriptive analyses of outcomes will be performed in the study population and in prespecified subgroups. Additionally, exploratory hierarchical regression models will be used to estimate associations with case and hospital characteristics.
Risk-Benefit analysis	The collection of routine anaesthesia care data in SUSTAIN-EUROPE poses no foreseeable risk to participants while delivering substantial benefit through a comprehensive, multicentre observation of anaesthesia practices across European hospitals.

List of abbreviations

CRF	Case report form
CTN	Clinical Trial Network
eCRF	Electronic case report form
ESAIC	European Society of Anaesthesiology and Intensive Care
FGF	Fresh gas flow
ICF	Informed consent form
ICH-GCP	International Council for Harmonisation - Good Clinical Practice
IRB	Internal review board
NC	National Coordinator
PI	Principal Investigator
SC	Steering committee
SOP	Standard operational procedure
TIVA	Total intravenous anaesthesia

1. ADMINISTRATIVE STRUCTURE

1.1 The Steering-writing committee

Linda Grüßer (University Hospital RWTH Aachen, Germany)
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András Keszei (Medical Faculty RWTH Aachen, Aachen, Germany);
Ana Kowark (University Hospital Bonn, Bonn, Germany);
Jan Larmann (University Hospital RWTH Aachen, Germany);
David van Meenen (Amsterdam UMC, Amsterdam, Netherlands);
Nicolaas H. Sperna Weiland (Amsterdam UMC, Amsterdam, Netherlands)

Statistician: András Keszei (Medical Faculty RWTH Aachen, Aachen, Germany)

1.2 Sponsorship

SUSTAIN-EUROPE is funded by a grant from the ESAIC Clinical Trials Network. ESAIC acts as sponsor, no other institution will be involved in conducting this study. ESAIC-CTN contact:
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2. BACKGROUND AND RATIONALE

2.1 Background

Climate change poses an escalating threat to global health.[1,2] It is estimated that the health care sector itself is responsible for 4.4% of global net emissions.[3] The perioperative environment, including anaesthesia, is highly resource-intensive, and everyday clinical decisions such as the choice of inhalational agent, fresh gas flow (FGF) settings, or the use of regional instead of general anaesthesia, affect the environmental footprint of anaesthetic practice.[4] Among all medical societies, anaesthetists were pioneers in taking responsibility by publishing recommendations to reduce the environmental impacts of their daily clinical routines.[5-9] These include the use of regional and total intravenous anaesthesia (TIVA) where possible and in inhalational anaesthesia cases, the use of sevoflurane and minimal FGF settings <0.5 l min^{-1}.[5] However, it is unclear if these recommendations are translated into daily routine. Guided by the principle "primum non nocere," it is essential to establish a comprehensive overview of current anaesthetic practices both to safeguard patient safety and public health, and to identify opportunities for further improvement.

Aligned with the ESAIC vision "Together for improved health outcomes, patient safety, and greater environmental sustainability across anaesthesiology and intensive care" this study is consistent with the World Health Organisation's Fourteenth General Programme of Work (2025–2028) "A Global Health Strategy for 2025–2028: advancing equity and resilience in a turbulent world,"[2] and directly supports the UN Sustainable Development Goal 3 (Good Health and Well-being) and Goal 13 (Climate Action)[10].

2.2 Rationale for the research project

Considering that an estimated 234 million major surgeries are performed globally each year, the limited data on real-world anaesthesia practices is surprising.[11] Available data on sustainable anaesthesia practices suggests considerable room for improvement.[12-16] For example, data from a U.S. nationwide database showed that while 25.5% out of 12.911.056 outpatient surgeries would have been amenable to peripheral nerve blocks, these were actually applied in only 3.3% of cases.[17] The use of regional anaesthesia in Europe remains largely unknown, with survey data indicating relevant heterogeneity on country level.[18] Similarly, regarding the use of TIVA versus inhalational anaesthesia, only survey data are available. In one survey, predominantly involving European respondents, 64% of 1285 anaesthetists preferred inhalational anaesthetics with sevoflurane used by 83% and desflurane by 10%.[12] Additionally, only 49% reported using FGF <1.0L min^{-1} in inhalational anaesthesia cases and only 15% reported FGF <0.5L min^{-1}.[12] Notably, while isolated paediatric quality improvement projects have demonstrated that implementation of sustainable anaesthesia practices is feasible,[19,20] there are no large studies assessing how anaesthesia is currently delivered in paediatric patients across Europe.

Sustainable anaesthesia practices in EUROPE – a multicentre, prospective observational study (SUSTAIN-EUROPE) is designed to close the knowledge gap on contemporary anaesthesia practices in both adult and paediatric populations. We aim to contribute to a better understanding of the status-quo in order to enable future studies on optimised, sustainable anaesthesia practices. Importantly, we aim to include all hospitals, not only

hospitals with dedicated research staff, but also hospitals from different clinical levels and from different countries representing the wide European spectrum. The goal is to better understand the reality of daily clinical routine in European hospitals.

3. OBJECTIVES AND ENDPOINTS

3.1 Objectives

SUSTAIN-EUROPE aims to describe the current anaesthesia practices used in paediatric and adult patients undergoing surgery or a procedure with anaesthesia care across Europe (including inhalational and total intravenous general anaesthesia, regional anaesthesia, sedation, and combinations thereof) in a large-scale, prospective, observational study. By providing information on the status-quo we seek to identify potential areas for improvement of sustainable practices that can be addressed in future studies.

3.2 Primary and secondary endpoint(s)

Primary endpoint:

- Type of anaesthesia (inhalational and total intravenous general anaesthesia, regional anaesthesia, sedation, combinations, monitoring only)

Secondary endpoints:

- Proportional use of kind of inhalational anaesthetics in inhalational anaesthesia cases
- FGF used stratified by TIVA and inhalational general anaesthesia; for inhalational cases further stratified by use of manual settings versus automated end-tidal dosing control
- MAC (age-adjusted), expiratory fraction and vaporiser settings in inhalational anaesthesia cases
- Proportion of kind of main i.v. medication used in TIVA cases
- Proportion of inhalational inductions
- Proportional use of inhalational agent capture and automated end-tidal dosing control
- Rebreathing fraction (FGF/expired minute volume ventilation) in general anaesthesia cases
- Among procedures anatomically amenable to regional anaesthesia alone, distribution of documented reasons for not using regional anaesthesia as the sole technique
- Use of depth of anaesthesia monitoring, corresponding values and availability of density spectral array
- MAC (age-adjusted) and depth of anaesthesia monitoring stratified by FGF rates
- Proportional use of antiemetics
- Ventilation settings in general anaesthesia cases including tidal volume kg^{-1} ideal body weight, ventilation pressures, fraction of inspired oxygen, respiratory rate, and end-tidal carbon dioxide

4. STUDY DESIGN

4.1 Type of research and general study design

SUSTAIN-EUROPE is a prospective, observational multi-centre study aiming to provide a standardized and contemporaneous snapshot of perioperative anaesthesia practices across Europe. During a predefined 5 consecutive working-day period, each participating department will record data on all eligible anaesthesia cases. For each case, information will be collected once intraoperatively or during the procedure, respectively.

4.2 Study centres and role of National Coordinators and local Principal Investigators

Any department of anaesthesiology within a hospital or medical centre in Europe is welcome to participate as a study centre. Study centre registration occurs online via a dedicated "Call for Centres form". Centres are responsible for confirming that adequate staffing is available during the recruitment period. National Coordinators (NC) and local principal investigators (PI) will coordinate all aspects of study implementation within their respective countries and sites.

NC are anaesthetists appointed by ESAIC and the Steering Committee (SC) to oversee the study within their countries. Their responsibilities include identifying and recruiting participating centres, supporting translation of study documents, ensuring that all national or regional regulatory approvals are in place, training and assisting local PIs, monitoring study conduct in line with ICH-GCP E6(R3), and maintaining communication with ESAIC headquarters and participating sites throughout all study phases, including data cleaning.

Local PIs are anaesthetists who lead the study at their institution. They are responsible for securing site-specific regulatory and ethical approvals, completing the pre-study questionnaire (Appendix 2), training relevant staff, supervising data collection, ensuring timely and accurate completion of the electronic case report form (eCRF, Appendix 3) and responding to data queries. By confirming data in the eCRF, the local PI attests to its integrity. Local PIs also maintain the investigator site file in accordance with ICH-GCP E6(R3) and communicate regularly with their NCs and ESAIC. All physicians obtaining informed consent (where required) and/or staff contributing to obtaining study data shall be familiar with the study protocol and procedures, as appropriate to their involvement. The local PI is responsible for ensuring that all staff are adequately informed about the study and that adherence to the protocol is maintained.

4.3 Procedures

Depending on local regulations and the approach to informed consent outlined in section 8.4, patients will either provide standard informed consent up to 90 days prior to surgery or the procedure, respectively, be consented postoperatively in the case of deferred consent, or be included under a waiver of individual consent. Data will be collected once on the day of surgery or the procedure, between 5 and 60 minutes after surgical incision or start of procedure, respectively. The term 'procedure' in this study refers to any diagnostic or interventional procedure requiring anaesthesia care, including but not limited to

endoscopic procedures, radiological interventions, and diagnostic imaging such as MRI. This time point was carefully chosen to promote methodological consistency across centres, to capture conditions reflecting a steady state while allowing the inclusion of short procedures, and to accommodate participation of centres with multiple hospital sites and varying research capacities. No additional procedures or follow-up are required. Data collection will be performed via a dedicated mobile application used by trained staff (details outlined in section 9.2). Depending on the type of data and local circumstances, data will be recorded directly from routine anaesthesia records, from the anaesthesia machine and from perioperative documentation.

Table 1: Summary table of the timings of assessments

When	Action/Parameters Collected
Day-90 to Day 0	Screening Inclusion/Exclusion criteria Consent if required*
Day 0	Case and anaesthesia characteristics

*or according to option 2 or 3 as outlined in section 8.4.

4.4 Recruitment and screening

Each centre may select a 1 week (= 5 consecutive working days) period within a one-year overall study inclusion window, ensuring that this period reflects standard clinical activity, i.e., it should not coincide with local holidays, major conferences, or other disruptions to routine scheduling. This time period can be adapted case by case upon chief investigators approval.

All consecutive eligible patients undergoing surgery during the selected inclusion period at each participating centre will be screened and, where required, invited to participate in the study.

The PI or designated members of the study team will be responsible for screening patients, obtaining informed consent from (ICF) eligible patients where required, and ensuring compliance with the study protocol and regulatory requirements. When informed consent is required, patients may be screened and invited to participate either at the preoperative clinic or on the day of surgery/procedure, as this is often the most practical option given local clinical structures and workflows. Various factors such as short-term scheduling changes, staffing constraints, or the organization of preoperative assessments can limit opportunities for earlier recruitment, making same-day inclusion both reasonable and ethically justified in this minimal-risk observational study. In case of deferred consent, consent may be obtained postoperatively as well.
These flexible approaches to recruitment ensure that a wide range of hospitals across diverse care settings can feasibly participate in SUSTAIN-EUROPE.

As part of the pre-hospital questionnaire (Appendix 2), each centre will report the average daily number of anaesthesia cases to provide a reference for estimating the proportion of eligible patients during the recruitment period. Centres should aim to recruit all eligible

patients; however, given the workload in large institutions and the pragmatic study design, not all may be screened. Centres should enter all patients they were able to screen in the eCRF (Appendix 3) presenting the convenience sample. Reasons for non-inclusion will be entered. At the end of the study period, each centre will complete an "End of Study Reporting Form" (see Appendix 4).

4.5 Methods of minimising bias

The key potential risks of bias in this pragmatic observational study are addressed as followed:

a) Selection bias: We attempt to minimise the risk of selection bias aiming for generalisable results by distributing the call for participation widely through ESAIC National Societies, and research networks. Furthermore, by simplifying recruitment and screening procedures, e.g., allowing each centre to select a recruitment period most applicable to their local circumstances, limiting the CRF to key data points, and offering the option of electronic data collection, we aim to reduce the workload particularly for smaller hospitals and thus facilitate broad participation across diverse healthcare settings. Selection bias at the patient level will be addressed by aiming to include all eligible patients within the selected inclusion period.
b) Performance bias: To reduce performance bias, data collection should be performed by staff members who are not directly responsible for the patient's intraoperative management. The anaesthesiology team will be informed about the data collection without disclosure of the specific study hypothesis to minimise the risk of a modified standard practice.
c) Detection bias: Data collection will be limited to objective variables that are routinely documented in daily practice and thus are familiar to every anaesthetist.

5. STUDY POPULATION

5.1 Inclusion criteria

All patients receiving any form of anaesthesia care (general or regional anaesthesia, monitored sedation, combinations thereof or monitoring only) from an anaesthetist at an anaesthesia workstation in participating European departments of anaesthesiology during the selected recruitment period.

5.2 Exclusion criteria

Patients (or legal guardians) who decline consent and patients for whom valid informed consent cannot be obtained due to language barriers or other factors preventing adequate information and understanding.

5.3 Criteria for withdrawal / discontinuation of participants

Participants may withdraw at any time; thereafter, no further data will be collected. All data obtained up to the point of withdrawal will remain pseudonymized and included in the analysis. Withdrawals will not be replaced.

6. STUDY ASSESSMENTS

6.1 Assessment of primary endpoint outcome

The type of anaesthesia (inhalational and intravenous general anaesthesia, regional anaesthesia, sedation, combinations, or monitoring only) will be recorded by a trained team member collecting data 5-60 minutes after skin incision or start of procedure, respectively. Depending on local workflow, data may be sourced from electronic anaesthesia records, the anaesthesia workstation display, paper-based charts or perioperative documentation. In the event that the anaesthetic approach changes intraoperatively, only the technique recorded at that time point will be used for analysis. Any local anaesthetic infiltration performed by the anaesthetist will be classified as regional anaesthesia, whereas if the surgeon alone administers local anaesthetic, this will not be classified by regional anaesthesia.

6.2 Assessment of secondary endpoints

All secondary endpoints, as defined above, will be recorded by a trained team member 5 – 60 minutes after skin incision or start of procedure, respectively. Depending on local workflow, data may be sourced from electronic anaesthesia records, the anaesthesia workstation display, paper-based charts or perioperative documentation.

6.3 Assessment of safety and reporting

As there are no study-related procedures, no additional safety monitoring beyond routine clinical care will be performed. All perioperative/periprocedural management, including any adverse events, will follow each centre's standard protocol routines. Serious adverse events are not applicable, because this is an observational study and no interventions are performed.

7. STATISTICAL METHODOLOGY

7.1 Sample size estimation

Based on sample size estimation for multinomial proportions[21] a sample size of 403 patients per country is needed to ensure a half width of 0.05 when calculating 90% confidence intervals for the proportions. We aim for a sample size of at least 8000 patients across at least 20 countries, which will allow us to achieve a reasonable precision for the estimation of the proportions of anaesthesia types in the study population and in subgroups of the study cohort. The study is observational and open to all eligible centres, so the final sample size and the number of countries may be higher or lower depending on recruitment. Regardless of the final number of participants, all predefined statistical analyses will be performed.

7.2 Planned analyses

7.2.1 Main analysis

Statistical analysis will be performed after the database cleaning process and database closure. Descriptive statistics will be used to report case and anaesthesia characteristics, proportion of non-response, and centre characteristics. Appropriate measures of central

tendency and variation, such as mean, median, standard deviation, quantiles and absolute and relative frequencies will be presented. Statistics will also be stratified by country, type and size of hospital and paediatric/adult populations. Exploratory hierarchical regression models will be fitted to assess adjusted outcome estimates and associations with case and hospital characteristics. Secondary outcome variables will be analysed in an exploratory manner using stratified descriptive statistics and appropriate graphical presentations. The final statistical analysis plan will be published before database cleaning process is finished.

7.2.2 Datasets to be analysed

The following datasets will be used for the analyses: dataset containing data of all adult participants, data of paediatric participants, data of participants receiving general anaesthesia, data of participants with inhalational anaesthesia and dataset of centre characteristics.

7.2.3 Handling of missing data

Absolute and relative frequencies of missing data will be tabulated for the study and stratified by country, type and size of hospital. Main analyses will be performed on the observed non-missing data. Since only routinely documented variables will be collected, missing patient data will be considered missing completely at random. Assumptions regarding missingness may be explored in sensitivity analyses.

7.2.4. Deviations from the original statistical plan

Any deviations from the pre-specified statistical analysis plan, which will be finalised and published prior to database lock, will be clearly documented and justified in all study reports. Any post-hoc analyses arising from these deviations will be explicitly labelled as such.

8. ETHICAL AND REGULATORY ASPECTS

8.1 Ethical Conduct of Study

The research project will be carried out in accordance with the research plan and the principles enunciated in the current version of the Declaration of Helsinki (amendment 2024) by the World Medical Association and the ICH-GCP Guidelines E6(R3). Specific national and local regulatory authority's requirements will be followed as applicable.

8.2 Risk categorisation

SUSTAIN-EUROPE is a multicentre, prospective, observational study assessing anaesthesia practices across different European hospital settings. No research related interventions are planned. All patients will receive routine care according to the standards of each participating institution. This study solely collects data arising from routine care, which itself is the focus of the investigation.

8.3 Institutional Review Board and Competent Authorities or equivalent

In all cases, prior to study initiation, the local PI at each centre must submit the study documents to the responsible Institutional Review Board (IRB), competent authorities or equivalent for ethical judgment and obtain document of proof that the study has been subject to IRB review and given approval/favourable opinion or exemption of patient

consent if applicable. After receiving IRB approval, it is mandatory that the study approval documentation coversheet (Appendix 5) is completed and signed by the local PI and sent back to ESAIC Research Department. If informed consent is not required by the local IRB, an explicit, written exemption must be obtained from the IRB. No substantial changes will be made to the protocol without prior IRB approval, except where necessary to eliminate apparent immediate hazards to study participants.

8.4 Participant Information and Informed Consent

Depending on local circumstances and institutional and legal requirements, the following approaches to participant information and informed consent will be employed:

1. **Standard informed consent**: For elective procedures, patients (or their legal representatives) will be informed prior to surgery and written informed consent will be obtained (up to 90 days before surgery) (Appendices 6B and 6C). For minors, informed consent will be obtained from parents or legal guardians according to national and institutional regulations. Where appropriate, an information sheet and assent form for minors may be used (Appendices 6E and 6F).
2. **Deferred consent**: In cases of emergency surgery, procedures (re-)scheduled on very short notice, or where preoperative consent was not feasible, patients (or their legal representatives) will be informed and asked for consent postoperatively. The patients will be informed postoperatively and asked for written informed consent as soon as their condition permits. For minors, consent will again be obtained from parents or legal guardians according to institutional and national regulations. Where appropriate, an information sheet and assent form for minors may be provided (Appendices 6E and 6F).
3. **Waiver of individual consent**: Where permitted by local ethical and legal frameworks, individual informed consent will be waived, as this study collects only limited pseudonymized data routinely generated during standard care, without any study-specific intervention or follow-up. In this case, the patient will receive the patient information sheet (Appendix 6A).

By relying exclusively on limited pseudonymized data routinely generated during standard care and foregoing any study-specific interventions, Option 3 not only prevents the substantial selection bias introduced by full written consent procedures[22], but also critically lowers the administrative burden that often precludes participation by smaller hospitals without dedicated research infrastructure. This inclusivity supports that both elective and emergency cases from a diverse range of sites are captured. Moreover, because only the minimum necessary data to evaluate anaesthesia practices are collected and the risk of patient re-identification is extremely low, the study poses negligible risk to participants. Implementation remains contingent on each site's IRB and data-protection committee approval and, where required by local regulation, may be complemented by a simple opt-out mechanism.

If local regulations require the use of Option 1 or 2, the following procedure will apply:
Patients (or their legal representatives or guardians) will receive and read the IRB-approved Informed Consent Form (ICF, Appendices 6A to 6F). Where established local electronic consent processes exist, e-consent via a validated, GDPR-compliant platform may be used

in lieu of paper consent. For elective cases, this will occur in the preoperative clinic or at the ward (up to 90 days before surgery), allowing ample time for review and questions. The investigator (or designee) will discuss study purpose, procedures, risks, benefits, data pseudonymization, confidentiality, voluntary participation and withdrawal rights; the participant signs and dates the ICF (or completes the e-consent workflow), receives a copy, and the original or digital record is filed. Enrolled patients, whose surgery is unexpectedly delayed more than 90 days after the preoperative visit, may be asked to give informed consent again.

In deferred-consent scenarios, the same information materials and discussion take place post-operatively as soon as the patient's condition permits, ideally within 21 days of surgery or the intervention, respectively. Signed forms or completed e-consent records are logged and handled identically to option 1. In all cases, no further data are collected after withdrawal, and all stored data remains pseudonymized.

The Sponsor provides templates of the participant's ICF for the main study and patient Information Sheet (in case of waiver) in English (see Appendices 6A to 6F). Each centre/country will have their own approved translated ICF according to the local legislation. All translations and adaptation of the ICFs should be sent to the Sponsor (ESAIC) for validation. Standard operating procedures (SOP) and guidance published by the Sponsor should be followed in this regard.

8.5 Participant privacy

ESAIC as the Sponsor and the investigator affirm and uphold the principle of the participant's right to privacy and shall comply with applicable privacy laws. Specifically, anonymity of the participants shall be guaranteed when presenting the data at scientific meetings or publishing them in scientific journals.

Individual subject medical information collected in this study is considered strictly confidential and disclosure to third parties is prohibited. Subject confidentiality will be further ensured by utilising subject identification code numbers and only pseudonymised data will be recorded in the central database.

For data verification purposes, authorised representatives of the sponsor or an ethics committee may require direct access to parts of the medical records relevant to the study, including participants' medical history.

8.6 Early termination of the study

SUSTAIN-EUROPE is an observational study. Therefore, premature termination of the study resulting from ethical or safety concerns is most unlikely. In case of insufficient participant recruitment, the study period may be extended to reach recruitment target.
In the unlikely event of premature study end or interruption of the study, a report will be sent to the IRB within 15 days, or as required. The regular end of the study is reported to the IRB within 90 days, the final study report shall be submitted within one year after study end, or as required. All communication, reports, and updates to the local IRB are the responsibility of the local PI.

8.7 Amendments, changes

Only the SC or persons delegated by the SC are entitled to amend the protocol. NCs and local PIs will receive timely notification of changes and will be required to submit amendments locally. Written approval of the amendment will be provided to the Sponsor and substantial amendments of the protocol will be only implemented after approval of the responsible IRB.
In consideration of the observational nature of the study, the necessity of protocol deviations to protect the rights, safety and well-being of human subjects without prior approval of the sponsor and the IRB appears remote. Such deviations must be documented and reported to the sponsor and the IRB as soon as possible.
Any amendments will be communicated to the IRB as necessary by the PI. It is the local PI responsibility to communicate with their IRB.

8.8 Risk-benefit assessment

This is a multicentre, prospective observational study that collects only data generated during routine clinical care. All data are pseudonymized. No additional procedures are performed, and patients will neither be approached for interviews nor followed up as part of the study. As such, there are no risks beyond data protection considerations. These will be mitigated by strict pseudonymisation, storage on secure servers located within the European Union, and controlled access governed by individual log-in credentials and gradated user rights, in full compliance with the GDPR (EU) 2016/679. The study poses minimal risk, while offering the potential benefit of providing a comprehensive observation of current anaesthesia across Europe, which may inform future quality improvement and sustainability initiatives.

9. GDPR, DATA AND QUALITY MANAGEMENT

9.1 Data quality

The sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs to ensure that the study is conducted and data are generated, documented (recorded), and reported in compliance with the protocol, ICH-GCP, and the applicable regulatory requirements.

Quality control measures will be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly, including written guidelines (in English for all countries) for data collection and entry, automated consistency checks, and training of NCs and local PIs. It will be the responsibility of the NC, with support by the study coordinating office, to train local PIs. Local PIs will ensure that the data in the eCRF are carefully entered and verified regularly. It will be the responsibility of local PIs to conduct periodic and random checks to ensure data quality in their centres. The sponsor will make random assessments of centres in order to confirm that there are no improper and incorrect data entered into the eCRF. On-site monitoring visits by the sponsor are not planned.

The sponsor is responsible for securing agreement from all involved parties to ensure direct access to all study related sites, source data/documents and reports for the purpose of monitoring and auditing by the sponsor, and inspection by domestic and foreign regulatory authorities. Any agreements, made by the Sponsor with the investigator/institution and any other parties involved with the study, will be in writing as a separate document. No fee or financial compensation is given to PI and/or participating institutions for patient recruitment.

9.2 Data handling and record keeping/archiving

Data will be collected at each centre, pseudonymised, and entered into the eCRF. Data will be entered into a secure online database protected by personal usernames and passwords and documenting the time and individual entering the data. Completed forms will be submitted to the sponsor, ESAIC Clinical Trials Network (ESAIC CTN), in Brussels, Belgium. The user should keep their log-in details confidential. The language of the online database, eCRF, and the relevant guidance are in English and will not be translated in the national languages.

For this multicentre, prospective observational study, data collection will be facilitated via a dedicated mobile application used by trained staff. Certain parameters, such as e.g., FGF, may be displayed on anaesthesia workstations but not routinely recorded in standard anaesthesia charts; in these cases, the values entered directly into the app by the observing staff constitute the source data, with the app's encrypted audit trail serving as the primary source documentation. In exceptional cases where data collection via the dedicated mobile application is not feasible, centres will record data directly into the paper CRFs and subsequently enter those data into the eCRF. A copy of every original source document, whether electronic or paper, will be retained in a locked cabinet or secure server area, accessible only to authorized personnel, in accordance with local and national regulations. Continuous audit trails within both the app and the eCRF will track all entries and modifications to ensure data integrity and accountability. In case of missing data, relevant variables may be retrieved retrospectively from routinely collected medical records, where available.

An identifiable patient data page (patient logsheet) reporting the assigned patient identification code will be stored separately (either digitally in a secure, access-restricted database or as a hard copy in a locked cabinet/office, per local capabilities) to support completion of missing data points, and to allow potential monitoring visits by NCs, Sponsor, IRB, or regulatory authorities. Signed consent forms, where required, will be retained as hard copies in a secure location or, where electronic consent is used, stored in a secure electronic system in accordance with local requirements. All study documents will be archived as required by local legislation. All collected data will remain the property of the Sponsor. Data will be stored 25 years in the central database. At the end of this period, the data will be destroyed or anonymized.

9.3 Confidentiality, data protection

To safeguard patients' confidentiality, a patient identification code will be assigned to encode data. The confidential log linking patient identification code and identifiable patient

data will be stored separately in a locked cabinet or secured server area accessible to authorised personnel only and corresponding electronic files will be protected by personalised and confidential usernames and passwords. eCRF are identified through the patient identification code and will not include any names, initials, date of birth, or local hospital patient numbers; therefore, no patient identifiable data will be directly accessible from the eCRF.
Data protection will be guaranteed through encoding and the use of a secured database with restricted access by individual log-in and gradated user rights. Further, only encrypted data will be stored centrally. The database will be hosted on servers physically located in the European Union. The data shall only be transferred to servers located in member States of the European Union or in other countries where the level of personal data protection has been determined as adequate by the European Commission on the basis of the GDPR (Article 45). In case request for future research purpose comes from a non-EU country, data can be transferred and ESAIC will ensure that either the country that receives the encoded-data is recognised as having an adequate level of data protection or appropriate safeguards will be put in place.

The results of the study will be used to answer the scientific questions of the study. In addition, collected data may be used for further research projects. These activities related to scientific or methodology improvement may include:

- planning new studies or improving analysis methods based on data from past studies
- publishing the research results in scientific journals or using them for educational purposes
- performing statistical analysis that combines the results of multiple scientific studies
- development of new research methodologies
- quality assurance and quality controls

Open direct access to all relevant trial information as well as source data/documents will be permitted for purposes of monitoring, audits or inspections to the Sponsor, NCs, IRB, or regulatory authorities. All handling of personal data will comply with the GDPR (EU) 2016/679, GCP Guidelines, and follow strictly the legal and applicable national requirements for data protection. The Sponsor may apply additional requirements, where applicable even if they are not expressly listed above. For any additional question please contact the ESAIC Data Protection Officer at privacy@esaic.org or 24, Rue des comédiens 1000 Brussels, Belgium.

10. PUBLICATION AND DISSEMINATION POLICY

10.1 Publication of results

The main results of SUSTAIN-EUROPE will be published in peer–reviewed international medical journals and presented at Euroanaesthesia and at national meetings. As recommended by the International Committee of Medical Journal Editors (Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals, updated version 2026, https://www.icmje.org/icmje-recommendations.pdf accessed June 2026) authorship will be considered based on:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
2. Drafting the work or reviewing it critically for important intellectual content; AND
3. Final approval of the version to be published; AND
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Based on their contributions, members of the SC and national coordinators will be considered as co-authors. Co-authors must fulfil all International Committee of Medical Journal Editors' authorship criteria (https://www.icmje.org/icmje-recommendations.pdf - Section 2) and recruit a substantial number of centres. Eligibility for authorship will be determined by the SC. The manuscript draft and submitted manuscript will be shared within the co-authors only. If journal-specific restrictions on the number of authors apply, an appropriate group authorship structure will be implemented.

All collaborators will be listed as in the "SUSTAIN-EUROPE Investigators" group. When submitting a manuscript, the corresponding author will include the group author name "SUSTAIN-EUROPE Investigators" as author in the byline. Since the group author name "SUSTAIN-EUROPE Investigators" is included in the byline as author and the individual names of the investigators are reported at the end of the paper or in an appendix, MEDLINE will list the individual names of the group members.

It is the responsibility of the local PIs to determine who is to be considered as investigator. The local PI will be asked to submit names of staff actively involved from their institution in the 'End of Study Reporting Form' (Appendix 4). If the number of recruited patients from a centre is too low to justify sufficient active involvement, the risk of bias may be too high, and the SC may decide on the legitimacy of the collaboration based on other contributions. The final decision will be left to the SC in consultation with the ESAIC.

The number of investigators allowed from each centre will be determined by the number of patients enrolled by that centre. This is described in Table 2 below.

Table 2: Number of investigators named according to number of patients enrolled and followed to completion within the recruitment period:

Number of patients completed	**Number of investigators at that centre**
>25	1
>50	2
>100	3
>150	4
>200	5
>250	6
>300	7
>450	8
…	…

Presentation at international meetings will be restricted to the members of the SC or their delegates. NCs will qualify for presentation at national meetings after approval by the SC and the sponsor. ESAIC Clinical Trial Network will be acknowledged in all publications and

presentations. It is also required for all publications to add the specific ESAIC Tracking ID ideally in the abstract (ESAIC_CTN_SUSTAIN-E).

10.2 Secondary analyses, sub-studies, and data sharing

Pre-defined sub-studies and secondary analyses aimed at exploring findings generated by the main study must be based on a pre-specified analysis plan (including authorship rules), comply with applicable local and European regulations, and receive approval from the SC before execution or reporting. After publication of the main results, each NC may also undertake additional analyses on their own country's dataset under the same conditions. Duplicate data publication is not permitted.
The final approval of potential secondary analyses and sub-studies rests with the SC. Prior to journal submission, any paper originating from the main data will be reviewed by the SC. Authorship of any secondary publication derived from the main data set will include the group name "SUSTAIN-EUROPE Investigators" and the names of the SC who have worked on the particular manuscript, with a by-line clearly stating that the individual names are elsewhere in the paper. For transparency, the original paper has to be referenced to in all articles of secondary analyses.

Local or national nested cohorts addressing additional questions, i.e. questions not addressed in SUSTAIN-EUROPE, and collecting additional data while sharing part of the variables collected for SUSTAIN-EUROPE, are allowed under the following conditions: nomination of a separate sponsor (i.e., other than the ESAIC), separate ethical approval, separate informed consent, independent data management, and approval of a detailed study proposal by the SC.

The Sponsor and the SC have the right to veto the nesting of a study into SUSTAIN-EUROPE. The publication of any study nested within SUSTAIN-EUROPE will occur after publication of the main results of SUSTAIN-EUROPE. For transparency, the original paper should be referenced to in all articles of nested analyses. Authorship rules for potential publications derived from such nested cohort studies are to be submitted to the Sponsor and SC together with the study proposal.
Requests for data sharing for individual-level meta-analyses are to be addressed to the Sponsor and SC.
The sponsor of the study (ESAIC CTN) can use pseudonymised pooled data for internal analyses and educational purposes.

11. FUNDING AND SUPPORT

SUSTAIN-EUROPE is sponsored by a grant from the ESAIC CTN. The submission for national or local peer-reviewed grants to fund national or local implementation of the study is allowed conditional on prior written authorization from the sponsor and the SC. The SC members declare not to have any conflicts of interest (a declaration of conflict of interest will be signed by each SC member and kept by the Sponsor).

12. INSURANCE

The study is purely observational and imposes no procedures beyond those already performed as part of routine clinical care; data collection is strictly limited to information generated during standard management.

Consequently, it is anticipated that no additional participant insurance is required beyond each site's standard clinical cover. In the rare jurisdictions where specific research or liability insurance is mandated by local regulation, PIs must verify and secure any necessary coverage.

The ESAIC has Public Liability insurance in place to cover the legal liability of the ESAIC as Sponsor in the eventuality of harm to a research participant arising from management of the research by the ESAIC staff. This does not in any way affect the responsibility of a centre for any clinical negligence on the part of its staff.

13. OTHER INFORMATION

ChatGPT (version 5.2) was used during the preparation of the study protocol and appendices for language editing and improving clarity. Suggested corrections were carefully double-checked and only applied where appropriate. All content and final responsibility remain with the SC and ESAIC.

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15. LIST OF APPENDICES

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16. PROTOCOL CHANGES HISTORY

Version Number	Change #	Page	Section	Description of changes