Finnish study of intraoperative irrigation versus drain alone after evacuation of chronic subdural hematoma (FINISH): Plan for the Statistical Analysis and Blinded Data Interpretation

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Trial registration number: NCT04203550
Study posted on ClinicalTrials.gov: December 18, 2019
Protocol published: June 21, 2020 (BMJ Open. 2020 Jun 21;10(6):e038275)
Actual patient recruitment time: January 1, 2020 to August 17, 2022
Final patient's 6 month follow-up date: February 17, 2023
Final statistical analysis plan (SAP): June 27–28, 2023
Final blinded data interpretation plan signed: June 27–28, 2023

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1. Introduction

To avoid bias in reporting and interpretation of the findings of the FINISH (Finnish Study of Intraoperative Irrigation Versus Drain Alone After Evacuation of Chronic Subdural Hematoma) trial, we, the Blinded Data Interpretation Committee have reached a consensus on how to carry out the statistical analysis and the blinded data interpretation. This document draft coined "**Minutes for FINISH statistical analyses and blinded data interpretation plan**" outlines the plan for the execution of the statistical analyses and blinded data interpretation of the FINISH trial.

Statistical analysis will be carried out by the trial statistician (TC) without any involvement from members of the Blinded Data Interpretation Committee or other FINISH investigators, as outlined below. The central study coordinator will code the trial data (two treatment arms) as "**Group A**" and "**Group B**" before handing the data over to the statistician, who performs the statistical analyses blind to the treatment allocation.

To reduce bias in the interpretation of the trial findings, blinded results from the intention-to-treat (ITT) and per-protocol (PP) analyses (Group A vs. Group B) will be presented to the Blinded Data Interpretation Committee. The Blinded Data Interpretation Committee will then contemplate on the possible interpretation based on two alternative scenarios, one where **Group A** is the "**irrigation group**" and one where **Group A** is the "**no irrigation group**". Only after the Blinded Data Interpretation Committee has reached a consensus on the proper interpretation of the findings, the central study coordinator will unblind the treatment group allocation.

Also, as Drs. Raj, Lönnrot. Luoto, Posti, Koivisto, Leinonen and Tetri, were involved in the clinical care of the patients, they will recuse themselves from making any interpretations but are to take part in the blinded data interpretation meeting to answer potential questions regarding the execution of the trial.

FINISH Blinded Data Interpretation Committee
Teppo LN Järvinen, MD, PhD (Chair)
Simo Taimela, MD, PhD (Co-chair)
Riku Kivisaari, MD, PhD (FINISH steering committee member)
Christoph Schwartz, MD, Associate Professor (University Hospital Salzburg, Austria)
Tomasz Czuba, trial statistician

FINISH trialists (recursed from interpretation)
Rahul Raj, MD, PhD
Kimmo Lönnrot, MD, PhD
Teemu Luoto, MD, PhD
Jussi P. Posti, MD, PhD
Timo Koivisto, MD, PhD
Ville Leinonen, MD, PhD
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Approval of the Statistical Analysis Plan and Blinded Data Interpretation
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Rahul Raj, MD, PhD

2. A brief overview of the FINISH trial

Patient/Population	Intervention (standard care)	Comparator (new treatment)	Outcome (primary)
Patients with symptomatic CSDHs requiring surgical burr-hole intervention	Burr-hole surgery with standard intraoperative subdural irrigation	Burr-hole surgery with no intraoperative subdural irrigation	Symptomatic CSDH requiring reoperation within 6 months

2.1 Background and Objectives

Chronic subdural hematoma (CSDH) is the most common type of intracranial hemorrhage and one of the most common diagnoses necessitating neurosurgical care. The incidence of CSDH is sharply rising due to diagnostic improvements and the aging population. The standard care for CSDHs in most countries is a surgical procedure called burr-hole evacuation (craniostomy), followed by intraoperative irrigation and placement of a subdural drain. However, there is a possibility that intraoperative irrigation may not be required, as it potentially leads to increased risks of infections, rebleeding, and patient distress during the procedure performed under local anesthesia. There is also evidence to suggest that irrigation *per se* may be harmful.

We conducted a pragmatic randomized, parallel-group, non-inferiority trial comparing burr-hole craniostomy with intraoperative irrigation and 48h of subdural drainage to the same treatment but with no intraoperative irrigation, with a primary objective to assess the therapeutic value of intraoperative irrigation. We chose the rates of reoperation in the two groups, as an indicator for recurrence of symptomatic CSDH within 6 months.

2.2 Design, Monitoring and Timetable

In this national five-center, stratified, block-randomized (block sizes 4, 6, 8) trial we randomized 587 patients to undergo burr-hole craniostomy of a CSDH in a 1:1 ratio. We compared the effect of burr-hole craniostomy with intraoperative irrigation followed by 48h (±12h) subdural drainage (irrigation group) and burr-hole craniostomy without intraoperative irrigation followed by 48h (±12h) subdural drainage (no irrigation group) on symptomatic CSDH recurrence requiring reoperation over the course of 6 month follow-up.

The full study protocol of the FINISH study has been published [1]. The trial was designed and conducted by the FINISH investigators and the analyses were completed at the coordinating center. The trial protocol was approved by ethical review at the institutional review board of the Helsinki and Uusimaa Hospital District on November 13, 2019 (HUS/3035/2019) and duly registered at ClinicalTrials.gov (https://clinicaltrials.gov/ct2/show/NCT04203550). All participants provided written informed consent. The trial was monitored by Clinical Research Unit of the Helsinki University Hospital (HYKS Institute), Helsinki, Finland. The writing committee of the FINISH trial vouch for the accuracy and completeness of the data, the fidelity of the trial to the protocol, and the complete reporting of adverse events. There was no industry involvement in the trial.

The FINISH trial was launched in the coordinating center (Helsinki) on January 1st, 2020. Due to the Covid-19 pandemic, the next centers joined with some delay, as follows: Oulu University Hospital in July 2020; Kuopio University Hospital in August 2020; Tampere University Hospital and Turku University Hospital in October 2020. All study centers retained in the trial until patient recruitment was completed on August 17, 2022.

2.3 Participants

During the recruitment period of the trial, we screened all patients with a symptomatic CSDH (CT or MRI verified) undergoing burr-hole evacuation in one of the study centers for trial eligibility.

The inclusion criteria were:

- Patients with a symptomatic unilateral or bilateral CSDH requiring burr-hole evacuation
    - Patients with bilaterally operated CSDHs will be treated with the same protocol on both sides and analyzed as a single study participant
- Predominantly hypodense or isodense on CT imaging (or chronic hematoma on MRI)
- Clinical symptoms correlating with the CSDH
- Patients older than 18 years of age

The exclusion criteria were:

- CSDH requiring surgical treatment other than burr-hole evacuation (eg, craniotomy)

- CSDH in a patient with a cerebrospinal fluid shunt
- Patients who had undergone any prior intracranial surgery
- Comatose patients (Glasgow Coma Scale (GCS) score ≤8) with absent motor responses to painful stimuli; decerebrate or decorticate posturing), where rapid hematoma evacuation was required
- postoperative cooperation was suspected to be insufficient for drain usage (ie, disoriented or semiconscious patient)
- had received active treatment for a haematogenic malignancy within the previous 5 years
- Patients with a central nervous system malignancy or tumor that may cause the patient's current symptoms or may interfere with the operation (eg, a small incidental meningioma without associated brain edema, not in the vicinity of the planned burr hole, was not an exclusion criterion)
- acute infection that required antibiotic treatment
- high risk of life-threatening thrombosis (eg, recent coronary stent, intracranial stent, recent pulmonary embolism, low-pressure cardiac valve replacement [mitral or tricuspid valve replacement]) and discontinuation of antithrombotic medication was not recommended

Screening logs were kept at all five centers until the end of the study (August 17, 2022). After being fully informed of the trial protocol, 588 eligible patients willing to participate (written informed consent from patient or next-of-kin) were randomized.

2.4 Randomization and Blinding

After informed consent, a member of the trial group carried out the randomization using an online eCRF system (Granitics Oy, Espoo, Finland). Due to the nature of the treatment, it was not possible to blind the surgeon and the OR staff from the treatment allocation. Measures to minimize bias included:

- The randomization was timed as closely as possible to the time of surgery (just prior to skin incision).
- Neither the patient nor the next-of-kin was informed of the treatment allocation.
- Treatment allocation was not documented in medical records (ie, all personnel participating in patient care after the operation were blinded to allocation).
- The study group members collecting postoperative data, outcome data, imaging data and performing the statistical analyses were blinded to treatment allocation over the entire course of the trial.
- The primary and secondary outcome measures were all evaluated in blinded matter, that is, the outcome assessors were blinded to treatment allocation.
- The study group committed to adhere to the blinded data interpretation analysis plan

2.5 Study Interventions

2.5.1 General surgical technique of the burr-hole surgery

The burr-hole craniostomy was done similarly in all centers, preferably under local anesthesia, with intravenous sedation with benzodiazepines and/ or opioids during the operation. General anesthesia was only used if the neurosurgeon or the anesthesiologist considered it unsafe to perform the procedure under local anesthesia. Routine preoperative antibiotic was given according to local protocols (normally a second-generation cephalosporin 30–60 min prior to incision). The surgeon drilled one 14 mm burr hole over the maximum convexity of the CSDH. In case of bilateral CSDHs, the surgeon performed the same procedure on both sides. If irrigation is used, after opening the dura, the surgeon irrigated the subdural collection with warm (body temperature) Ringer's lactate saline until rinsing appeared clear or at least 200mL (in case of bilateral CSHD, 200 mL per side, i.e., 400 mL total). After that, the surgeon inserted a subdural drain 3–5 cm deep and parallel to skull. The position of the drain (anterior, posterior) was left to the discretion of the surgeon. Burr hole covers or hemostatic were not routinely used (e.g., Spongostan, Tachosil). The type of subdural drain was not standardized, but all study centers used 10F drains applicable for subdural use. Following drain insertion, the proximal end was tunneled approximately 4–5cm from the incision and connected to a passive ventricular drainage bag (through a non-return valve) and the skin incision was closed in two layers (normally absorbable 3–0 suture for subcutis/galea and non-absorbable 4–0 suture for skin). The drain was fixed to the skin in a secure way. The drain-to-skin fixation technique was left to the discretion of the surgeon. The drainage bag was positioned at bed level. The duration of subdural drainage was 48 hours (±12hours) [2,3]. Patient mobilization was allowed during drainage (drain is kept open). Prophylactic antibiotics during drainage are not routinely used.

2.5.2 Irrigation group

The burr-hole craniostomy was performed as described earlier. The dura was sharply opened, and 10 mL of subdural exudate was aspired with a blunt aspiration needle for storage at −75°C to be used for later analysis. The subdural space was irrigated by repeated rinsing with body temperature saline solution with a syringe and blunt

needle until the surgeon considered the exudate to be clear. The minimum irrigation volume was 200 mL per operated side. The subdural drain was inserted 3–5 cm subdurally. Thereafter, the operation was completed as described earlier.

2.5.3. No irrigation group

A burr-hole craniostomy was performed as described earlier. A small incision in the dura was made and 10mL of subdural exudate was aspired with a blunt aspiration needle for storage at −75°C to be used for later analysis. Directly thereafter, the subdural drain was inserted approximately 3–5 cm subdurally. Thereafter, the operation was completed as described earlier.

2.6 Primary (efficacy) outcome measure

The primary outcome measure was the rate of reoperations of ipsilateral CSDHs within 6 months.

During the execution of the trial, the decision to reoperate was left at the discretion of the neurosurgeon on-call but enforced to adhere to the standard indications of CSDH, thus being identical to indications used for the primary operation (i.e., symptom recurrence or insufficient resolution of clinical symptoms correlating to imaging findings [CT or MR imaging]). All reoperations were conducted according to the current standard of care (burr-hole with irrigation and subdural drain placement). Knowledge of the group-assignment (whether or not irrigation was carried out in the primary CSDH surgery) was not considered necessary and accordingly, unblinding was not carried out prior to or after reoperation.

2.7 Secondary outcome measures

Originally, the FINISH trial was not powered for secondary outcome measure comparisons and these outcomes were considered exploratory (apart from the exception outlined regarding mortality and mRS in the Blinded Data Interpretation). The secondary outcomes included:

- Modified Rankin Scale at 6 months after the operation
- Mortality within 6 months of operation (all-cause mortality)
- Duration of the operation
- Hospital length of stay (index hospital and need for further care)
- CSDH volume reduction at 2 months after the operation
- Adverse events (minor adverse event [MAE], severe adverse event [SAE], procedure-related adverse event [PRAE]

The modified Rankin Scale (mRS) is a validated instrument used to evaluate the level of disability or dependence in individuals with neurological impairments in their activities of daily living [4]. The score ranges from 0 to 6:

0 No symptoms
1 No significant disability despite symptoms; able to carry out all usual duties and activities
2 Slight disability; unable to carry out previous activities, but able to look after own affairs without assistance
3 Moderate disability; requiring some help, but able to walk without assistance
4 Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5 Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6 Dead

2.8 Definition of adverse events

Safety endpoints within 6 months of operation, including the number and severity of adverse events (AE) and procedure-related adverse events (PRAE). Adverse events are categorized as serious adverse events (SAE) and minor adverse events (MAE). We decided to report procedure-related (severe and minor) adverse events separately.

SAE was defined as any inappropriate medical occurrence or effect that results in death, is life-threatening, requires hospitalization or prolongation of an existing inpatient hospitalization, results in persistent or significant disability or incapacity, or is another important medical event.

- Life-threatening in the definition of SAE refers to an event when the patient was at risk of death at the time of the event and does not refer to an event where the event might have hypothetically caused death. Prolonged hospitalization due to delayed transfer will not be considered an AE or SAE.

- Examples of SAEs are death, acute myocardial infarction, pulmonary embolism, systemic infection, acute cerebral infarction (PRAE), intracranial infection (PRAE), epileptic seizures (PRAE) and acute postoperative intracranial hematoma (PRAE).

MAE was defined as clinically mild manifestations, such as the patient possibly being aware of the event or symptom but the event or symptom is easily tolerated by the patient.

- Examples of MAEs are local wound infections manageable with oral antibiotics (PRAE), abnormal skin bleeding from the wound (PRAE), other local infections manageable with oral antibiotics and deep venous thrombosis not causing pulmonary embolism.

2.9 Sample size

2.9.1 Original sample size calculation

The original sample size calculation was presented in the protocol as follows [1]:

The trial is designed to ascertain whether drain without irrigation is non-inferior to drain with irrigation, with the rate of reoperations of ipsilateral CSDHs within 6 months as the primary outcome. We based the standard rate of reoperations (9.6%) on the results from a recent Cochrane review that reported the recurrence rates after CSDH evacuation followed by subdural drainage in six randomized controlled trials (RCTs) with more than 30 patients per treatment arm [5]. This yielded a maximum allowed margin of 9.0% to achieve non-inferiority. Following a consensus meeting with the trial investigators, the non-inferiority margin was lowered to 7.5%. Thus, with a non-inferiority margin of 7.5%, a 2.5% level of statistical significance (alpha=0.025) and an 80% power (beta=0.20), we will need 243 patients per study group [6]. Accounting for a drop-out rate of 10%, the required group size increases to 270 per study group. Accordingly, we set the recruitment target at 540 patients.

2.9.2 Final sample size calculation

After recruiting 80% of the 540 patients on January 23, 2022, there were a total of 68 patients (15.7%) with a protocol violation (referred to as "non-adherence"). The non-adherences were due to subdural drainage time less than 36h (n=42), no subdural drain inserted (n=13), subdural drainage time more than 60h (n=7), no drainage time information (n=3), no information regarding the surgical procedure (n=1), craniotomy performed (n=1), treatment cross-over (n=1). A non-adherence rate of 15.7% was higher than the originally assumed 10%. As the higher than anticipated non-adherence rate negatively affects the power of the per-protocol analysis, which is specified of equal importance to the intention-to-treat analysis by the European Medicines Agency [7], we presented the issue to the Data and Safety Monitoring Board (DSMB) on March 1, 2022. After contemplation, the DSMB recommended that the sample size would be recalculated to compensate for the higher than anticipated non-adherence. Prompted by this, we held a meeting with Professor Gordon Guyatt (Department of Clinical Epidemiology and Biostatistics, McMaster University) on April 01, 2022, on the most appropriate course of action. Professor Guyatt recommended a recalculation of the sample size – with a possibility to increase recruitment – to adjust for the higher than anticipated non-adherence rate.

The recalculated sample size is 578 patients (289 patients per group). This is calculated as follows:

$$\frac{486}{1-0.157} = 576.51.. = 578$$

The full description of the recalculated sample size is found in the minutes of "FINISH Principal Investigators Meeting 05/04/2022" below:

FINISH Finnish Intraoperative Irrigation Study for Chronic Subdural Haematoma Evacuation

FINISH Principal Investigators Meeting

Meeting on sample size recalculation

05/04/2022

1. Opening the meeting
A meeting between the principal investigators of the centers participating in the FINISH trial was held on 05/04/2022 in Microsoft Teams 13:00 UTC. The meeting began at 13:07 UTC.

Present:
Kimmo Lönnrot (principal PI)
Jussi P. Posti (TYKS PI)
Timo Koivisto (KYS PI)
Ville Leinonen (KYS PI)
Teemu Luoto (TAYS PI)
Teemu Luostarinen (steering group member)
Rahul Raj (methods/HUS PI)

Not present:
Sami Tetri (OYS PI)

The meeting agenda was presented by RR and KL.

2. Discussing the sample size and possible recalculation
RR opened the meeting by repeating the rationale for the initial sample size calculation that yielded a total study population of 540 patients (270 patients per group). In the initial sample size calculation, the following assumptions were made: reoperation rate=9.6%, alpha=2.5%, beta=20% (power=80%), non-inferior margin=7.5% (see study protocol for details). This yielded a total of 486 patients. A 10% dropout rate was added, to compensate for dropouts, yielding a total sample size of 540 patients.

After 80% of the 540 patients had been recruited and randomized on 23/01/2022, there were a total of 68 patients (15.7%) with a protocol violation (referred to as “non-adherence”). The most common reason for non-adherence was subdural drainage under 36h (n=42), no subdural drain inserted (n=13), subdural drainage time over 60h (n=7), no drainage time information (n=3), no surgery information (n=1), craniotomy (n=1), group cross-over (n=1).

A non-adherence rate of 15.7% is higher than the originally assumed 10%. The higher than anticipated non-adherence rate would negatively affect the power of the per-protocol analysis, which is of equal importance to the intention-to-treat analysis, as specified by the European

Medicines Agency and by the FINISH study protocol. A non-adherence rate of 15.7% translates into 455 patients treated per-protocol after recruiting 540 patients. Thus, the per-protocol analysis would be underpowered (455/486=93.6%).

The subject has previously been discussed with the data and safety monitoring board (DSMB) on 01/03/2022. The DSMB recommended that the sample size would be recalculated to compensate for the higher than anticipated non-adherence. The subject was also discussed with Professor Gordon Guyatt (Department of Clinical Epidemiology and Biostatistics, McMaster University) on 01/04/2022. He also recommended a recalculation of the sample size to adjust for the higher than anticipated non-adherence rate.

The recalculated sample size is 578 patients (289 patients per group). This is calculated as follows:

$$\frac{486}{1-0.157} = 576.51.. = 578$$

4. Deciding on the sample size and recalculation
All participants unanimously agreed to recalculate and increase the sample size from 540 patients to 578 patients. The current recruitment pace has been approximately 20 patients per month. The recalculated sample size (+38 patients) translates into an addition of 2 months of recruitment. This was considered reasonable by all participants.

5. Deciding on the next meeting and recruitment termination
The next meeting will be held in the mid/end of August 2022. By then we will assess the current sample size and possible recruitment termination whether full sample size has been reached. As of 05/04/2022, the number of patients recruited (intention-to-treat group) is 503/578 (87%).

4. Closing the meeting
The meeting was closed at 13.30 UTC.

3.0 Summary of changes to the original protocol

Original	Final
The study was not powered for secondary outcome measure comparisons and these outcomes were considered exploratory. The secondary outcomes included: - Modified Rankin Scale at 6 months after the operation - Mortality within 6 months of operation (all-cause mortality) - Duration of the operation - Hospital length of stay (index hospital and need for further care) - CSDH volume reduction at 2 months after operation	The study was not powered for secondary outcome measure comparisons and these outcomes were considered exploratory apart from the exception outlined above regarding mortality and mRS in the Blinded Data Interpretation. The secondary outcomes included: - Modified Rankin Scale at 6 months after the operation - Mortality within 6 months of operation (all-cause mortality) - Duration of the operation - Hospital length of stay (index hospital and need for further care) - CSDH volume reduction at 2 months after operation - Adverse events (minor adverse event [MAE], severe adverse event [SAE], procedure-related adverse event [PRAE]
Accounting for a drop-out rate of 10%, required group size increases to 270 per study group. Accordingly, we set the recruitment target at 540 patients.	A non-adherence rate of 15.7% was higher than the originally assumed 10%. The recalculated sample size is 578 patients (289 patients per group). This is calculated as follows: $\frac{486}{1-0.157} = 576.51.. = 578$

3. Statistical analysis plan (SAP)

3.1 Original statistical analysis plan

The original plan for the statistical analyses was presented in the trial protocol as follows [1]:

The statistical analysis will be performed both according to intention-to-treat (ITT) and PP principles. We will claim non-inferiority of single burr-hole evacuation without irrigation and subdural drainage only if this outcome is supported both by the ITT and the PP analysis. The ITT analysis will be performed using the full analysis set (FAS), defined as all randomized patients in the groups allocated to by the randomization. No exclusions other than caused by missing information will be made. No imputation will take place. The PP analysis will be performed on the subset of the FAS that is compliant with the protocol, have a completed treatment, available measurements and no major protocol violations nor entry criteria violations.

Summary statistics will be presented for both groups. Continuous variables will be presented in terms of mean values or medians with SDs and IQRs, respectively. Categorical variables will be presented with relative frequencies in percent.

The results from the statistical analysis will be considered to support a claim of non-inferiority if the upper limit of a one-sided 97.5% CI (or equivalently a 95% two-sided CI) excludes a difference in the primary endpoint in favor of the IR of more than 7.5%. The center stratification of the randomization will be accounted for in the calculation of the CI.

Exploratory analyses of secondary and other binary endpoints will be performed using the χ^2 test or logistic regression analysis. Continuous outcomes will be analyzed using Student's t-test or analysis of covariance. Potential effect modifiers (patient age, unilateral vs bilateral CSDH, use of antithrombotic medication, preoperative mRS and preoperative clinical status, hematoma density, hematoma size and presence of membranes on preoperative imaging) will be analyzed by including interaction terms in statistical models.

The primary endpoint will be investigated as described above using a CI, which is equivalent to using a non-inferiority test with a one-sided p-value of 0.025 (or a two-sided of 0.05). The statistical testing of other endpoints will also be performed using a two-sided significance level of 0.05. The statistical analysis will be performed using appropriate statistical software packages.

Prior to the statistical analysis, a statistical analysis plan will be finalized and an independent statistician will approve a dataset with sufficient data quality for the statistical analysis. Another statistician blinded to treatment arm will perform the analyses.

3.2 Final statistical analysis plan

The primary outcome for efficacy is the rate of symptomatic CSDH ipsilateral recurrences requiring reoperation within 6 months. The statistical analysis for efficacy will be performed according to both the ITT and PP principles. The ITT analysis will be performed using the full analysis set, defined as all randomized patients in the groups allocated by randomization. No exclusions other than those caused by missing information will be made. No imputation will take place. The PP analysis will be performed on the subset of the full analysis set that is compliant with the protocol, has completed treatment, has available measurements, and has no major protocol violations or entry criteria violations.

As the goal of CSDH surgery is not only to prevent reoperations but also to improve neurological function and prevent death, the entire therapeutic effect (value) of intraoperative irrigation (versus no irrigation) may not be sufficiently comprehensively captured by analysing the primary outcome (rate of reoperations) only. For example, any possible between-group differences in the incidences of deaths and unfavorable functional outcomes may have an effect on the likelihood of a patient being considered for reoperation (i.e., skew the primary analysis).

Prompted by this realization, we deemed it necessary to somehow take into account between-group differences in either mortality and/or unfavorable functional outcome (mRS 0–3 vs. 4–6) in interpreting the findings of the FINISH trial. The approach, to be used in the blinded data interpretation (BDI) [8] of the FINISH trial, is outlined below. In addition, in the event that we will observe a statistically significant difference in the number of deaths

between the two groups, we will carry out a detailed analysis of the causes of death by examining the official death certificates of the participants.

We will claim treatment non-inferiority only if:

1) Our primary efficacy analysis, based on the primary outcome, shows non-inferiority and the finding is supported both by the ITT and the PP analyses,

and

2) there are no relevant between-group differences in mortality (alive or dead at 6 months) or unfavorable functional outcome (mRS 0–3 vs. 4–6 at 6 months) between the groups (according to an approach outlined in the BDI).

Summary statistics will be presented for both groups. Continuous variables will be presented in terms of mean values or medians with SDs and IQRs, respectively. Categorical variables will be presented with relative frequencies in percent.

The results from the statistical analysis will be considered to support a claim of non-inferiority if the upper limit of a one-sided 97.5% CI (or equivalently a 95% two-sided CI) excludes a difference in the primary endpoint in favor of the irrigation group of more than 7.5%. The center stratification of the randomization will be accounted for in the calculation of the CI.

Exploratory analyses of secondary and other binary endpoints will be performed using the χ^2 test or logistic regression analysis. Continuous outcomes will be analyzed using regression Student's t-test, analysis of covariance or regression models.

Potential effect modifiers will be analyzed by including interaction terms in statistical models for the following subgroups:

- patient age (<70 years, ≥70 years)
- GCS score at baseline (9–12, 13–14, 15)
- history of head trauma (<4 weeks, ≥4 weeks, head trauma with unknown timing, no head trauma)
- unilateral versus bilateral CSDH
- use of anticoagulation and/or antiplatelet medication versus none
- preoperative mRS (0–3, 4–5)
- hematoma density (isodense, mixed-density, hypodense)
- hematoma size (width in mm)
- presence of membranes on preoperative imaging (yes, no)

The primary endpoint will be investigated as described above using a CI, which is equivalent to using a non-inferiority test with a one-sided p-value of 0.025 (or a two-sided of 0.05). The between-group comparison of 6-month mortality and mRS 4–6 differences will be compared using 85% and 95% CIs (as outlined in more detail in the BDI). The statistical testing of other endpoints will also be performed using a two-sided significance level of 0.05.

STATA (Statistics/Data analysis, SE v15.1, StataCorp LLC, 4905 Lakeway Drive, College Station, Texas 77845 USA) will be used for analyses.

3.3 Summary of changes to the original statistical analysis plan

Original	Final
We will claim non-inferiority of single burr-hole evacuation without irrigation and subdural drainage only if this outcome is supported both by the ITT and the PP analysis.	We will claim treatment non-inferiority only if: 1) Our primary efficacy analysis, based on the primary outcome, shows non-inferiority and the finding is supported both by the ITT and the PP analyses, and

	2) there are no relevant between-group differences in mortality (alive or dead at 6 months) or unfavorable functional outcome (mRS 0–3 vs. 4–6 at 6 months) between the groups (according to an approach outlined in the BDI).
Exploratory analyses of secondary and other binary endpoints will be performed using the χ^2 test or logistic regression analysis. Continuous outcomes will be analyzed using Student's t-test or analysis of covariance.	Exploratory analyses of secondary and other binary endpoints will be performed using the χ^2 test or logistic regression analysis. Continuous outcomes will be analyzed using regression Student's t-test, analysis of covariance or regression models.
Potential effect modifiers (patient age, unilateral vs bilateral CSDH, use of antithrombotic medication, preoperative mRS and preoperative clinical status, hematoma density, hematoma size and presence of membranes on preoperative imaging) will be analyzed by including interaction terms in statistical models.	Potential effect modifiers will be analyzed by including interaction terms in statistical models for the following subgroups: - patient age (<70 years, ≥70 years) - GCS score at baseline (9–12, 13–14, 15) - history of head trauma (<4 weeks, ≥4 weeks, head trauma with unknown timing, no head trauma) - unilateral versus bilateral CSDH - use of anticoagulation and/or antiplatelet medication versus none - preoperative mRS (0–3, 4–5) - hematoma density (isodense, mixed-density, hypodense) - hematoma size (width in mm) - presence of membranes on preoperative imaging (yes, no)
	The between-group comparison of 6-month mortality and mRS 4–6 differences will be compared using 85% and 95% CIs (as outlined in the BDI).

The final SAP plan was approved by:

Rahul Raj (Jun 27, 2023 00:01 GMT+3) Jun 27, 2023

Rahul Raj (SCM, methods PI)

Tomasz Czuba (Jun 28, 2023 10:49 GMT+2) Jun 28, 2023

Tomasz Czuba (trial statistician)

Kimmo Lönnrot (Jun 27, 2023 07:13 GMT+3) Jun 27, 2023

Kimmo Lönnrot (SCM, trial PI)

Simo Taimela (Jun 27, 2023 23:06 GMT+3) Jun 27, 2023

Simo Taimela (SCM, BDI committee co-chair)

Teppo Järvinen (Jun 27, 2023 10:56 GMT+3) Jun 27, 2023

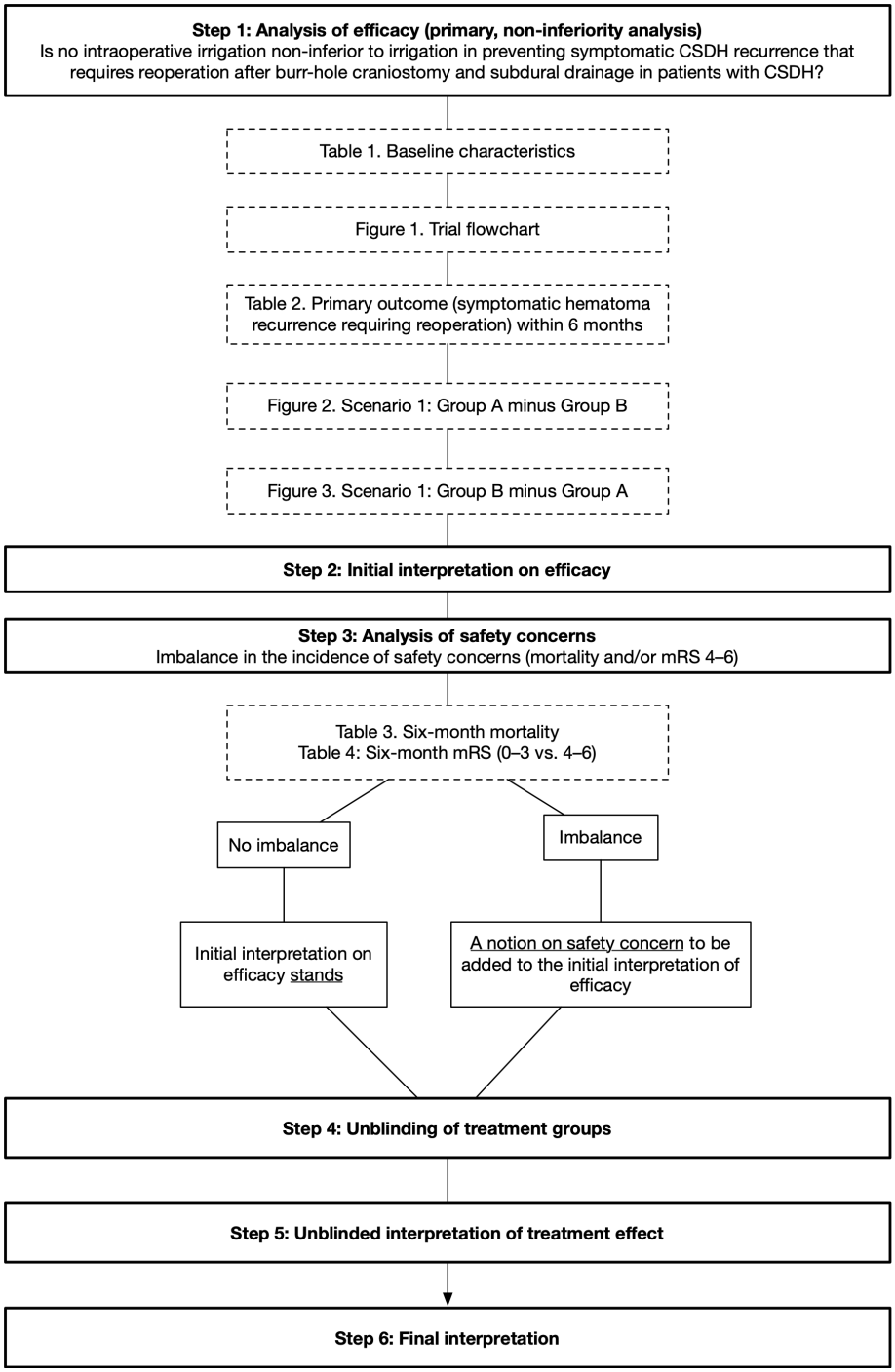
Teppo LN Järvinen (SCM, BDI committee chair)

**SCM = Steering Committee Member of the FINISH trial*

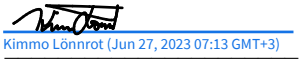
4. Blinded data interpretation (BDI)

The data will be interpreted according to a blinded data interpretation scheme we have published and described in detail previously [9]. In brief, the FINISH statistician (TC) will carry out the statistical analyses, blinded to the group assignment, and presents the data as Group A and Group B. The FINISH Blinded Data Interpretation committee will then contemplate the blinded results until a consensus on the interpretation is reached. Once the Blinded Data Interpretation committee reaches a consensus, the data will be unblinded and no changes are made to the interpretation of the results.

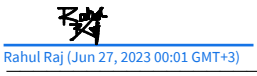
The sequence of events to take place in the upcoming 'blinded data interpretation meeting' is outlined in the flow chart below:



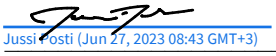
The final BDI plan was approved by:


Kimmo Lönnrot (Jun 27, 2023 07:13 GMT+3) Jun 27, 2023

Kimmo Lönnrot (trial PI)


Rahul Raj (Jun 27, 2023 00:01 GMT+3) Jun 27, 2023

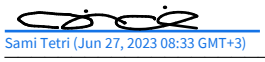
Rahul Raj (local PI, SCM)


Jussi Posti (Jun 27, 2023 08:43 GMT+3) Jun 27, 2023

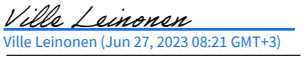
Jussi Posti (local PI, SCM)


Teemu Luoto (Jun 28, 2023 15:02 GMT+3) Jun 28, 2023

Teemu Luoto (local PI, SCM)


Sami Tetri (Jun 27, 2023 08:33 GMT+3) Jun 27, 2023

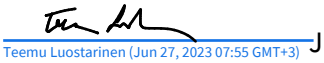
Sami Tetri (local PI, SCM)


Ville Leinonen (Jun 27, 2023 08:21 GMT+3) Jun 27, 2023

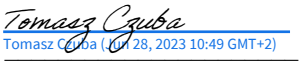
Ville Leinonen (local PI, SCM)


Timo Koivisto (Jun 27, 2023 14:13 GMT+3) Jun 27, 2023

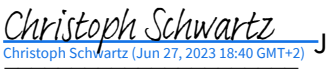
Timo Koivisto (SCM)


Teemu Luostarinen (Jun 27, 2023 07:55 GMT+3) Jun 27, 2023

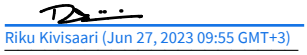
Teemu Luostarinen (SCM)


Tomasz Czuba (Jun 28, 2023 10:49 GMT+2) Jun 28, 2023

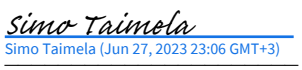
Tomas Czuba (trial statistician)


Christoph Schwartz (Jun 27, 2023 18:40 GMT+2) Jun 27, 2023

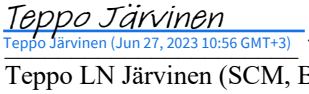
Christoph Schwartz (BDI committee member)


Riku Kivisaari (Jun 27, 2023 09:55 GMT+3) Jun 27, 2023

Riku Kivisaari (SCM, BDI committee member)


Simo Taimela (Jun 27, 2023 23:06 GMT+3) Jun 27, 2023

Simo Taimela (SCM, BDI committee co-chair)


Teppo Järvinen (Jun 27, 2023 10:56 GMT+3) Jun 27, 2023

Teppo LN Järvinen (SCM, BDI committee chair)

**SCM = Steering Committee Member of the FINISH trial*

Minutes of the BDI
[BLINDED VALUES TO BE ADDED BY TRIAL STATISTICIAN PRIOR TO THE BDI MEETING]

Step 1: Analysis of efficacy (primary, non-inferiority analysis)

Is no intraoperative irrigation non-inferior to irrigation in preventing symptomatic CSDH recurrence that requires reoperation after burr-hole craniostomy and subdural drainage in patients with CSDH? Based on the data in Table 2 and Figures 2 and 3, we will make an initial (blinded) interpretation on efficacy. Table 1 below describes the baseline characteristics of the study population.

Table 1. Baseline characteristics of the participants randomly assigned to irrigation or no irrigation.

Characteristic	Group A (n=??)	Group B (n=??)
Age – yr		
Female sex – no./total no. (%)		
Medical comorbidities – no./total no. (%)		
Diabetes mellitus		
Cardiac arrhythmia		
Previous cerebrovascular event		
Hypertension		
Ischemic heart disease or peripheral artery disease		
Cardiac valve prosthesis		
Pulmonary embolism or deep vein thrombosis*		
Dementia		
History of head trauma – no./total no. (%)		
Yes		
No		
Unknown		
Preoperative use of antithrombotic medication – no./total no. (%)		
No		
Antiplatelet		
Anticoagulant		
Symptoms at admission– no./total no. (%)		
Gait disturbance or falls		
Hemiparesis		
Speech disturbance		
Cognitive impairment		
Headache		
Seizure		
Other		
GCS at admission – no./total no. (%)		
15		
13–14		
9–12		
mRS at admission – no./total no. (%)		
1–3		
4–5		
Midline shift – mm		
Hematoma laterality† – no./total no. (%)		
Unilateral		
Bilateral		
Hematoma width, mm – mean (sd)		
Unilateral		
Bilateral‡		
Hematoma density§ – no./total no. (%)		
Isodense		
Hypodense		
Mixed density		
Hematoma membranes§ – no./total no. (%)		
Yes		
No		

* within 12-months before admission
† patient may have a hematoma not operated on
‡ sum of left and right hematoma widths
§ presented as individual hematomas
Abbreviations: GCS=Glasgow Coma Scale, mRS=modified Rankin Scale, SD=Standard Deviation, yr=years

Figure 1. Trial flow chart.

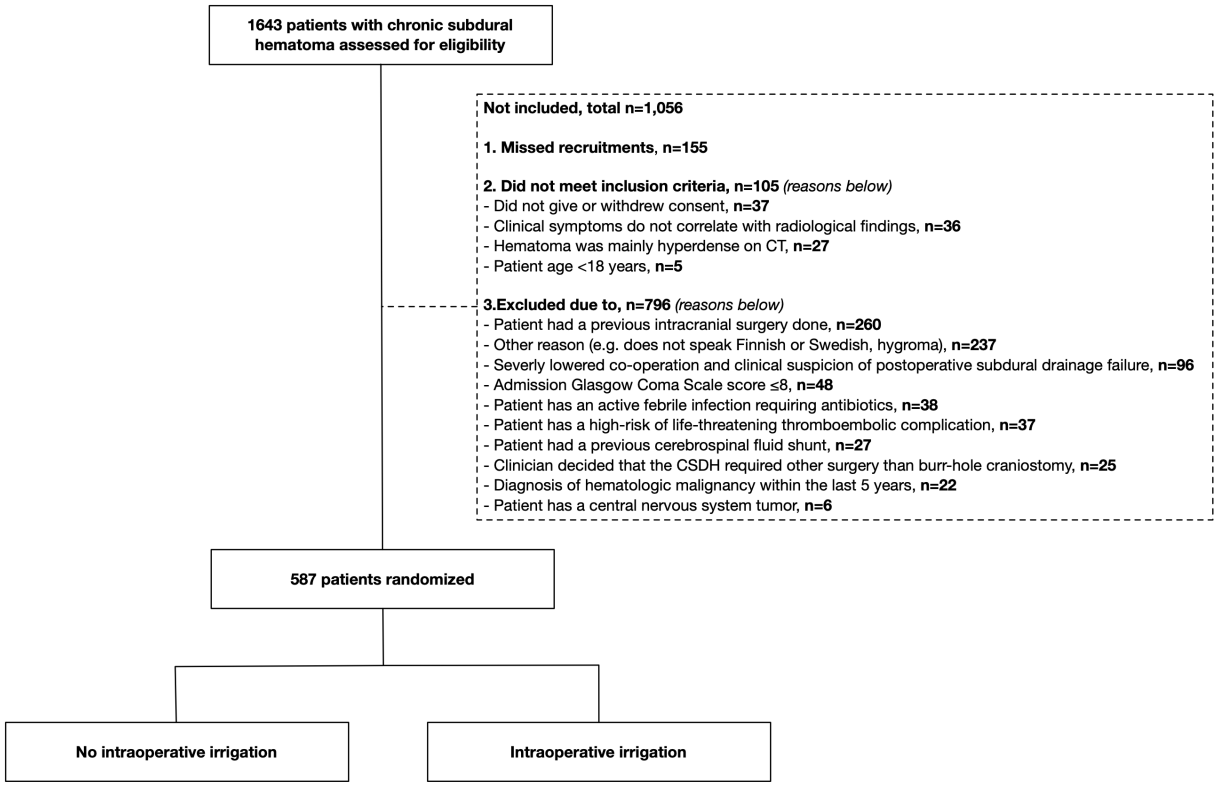
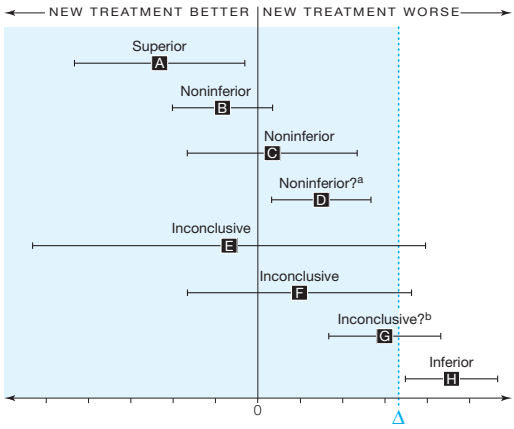


Table 2. Primary outcome at the primary outcome assessment time point (6 months).

Variable	Group A	Group B	Difference (97.5% CI)	P-value
Intention-to-treat	n=??	n=??		
Secondary surgery for recurrent CSDH	??/n (x%)	??/n (??%)	x (x to x)	??
Per-protocol-treated	n=??	n=??		
Secondary surgery for recurrent CSDH	??/n (x%)	??/n (??%)	x (x to x)	??

Abbreviations: CSDH=chronic subdural hematoma, CI=confidence interval

Our judgment on the efficacy (non-inferiority) will be based on the location of the whole CI in relation to Δ (non-inferiority margin) [10].



Error bars indicate 2-sided 95% CIs. The blue dashed line at x=Δ indicates the noninferiority margin; the blue tinted region to the left of x=Δ indicates the zone of inferiority. A, If the CI lies wholly to the left of zero, the new treatment is superior. B and C, If the CI lies to the left of Δ and includes zero, the new treatment is non-inferior but not shown to be superior. D, If the CI lies wholly to the left of Δ and wholly to the right of zero, the new treatment is noninferior in the sense already defined but also inferior in the sense that a null treatment difference is excluded. This puzzling circumstance is rare, because it requires a very large sample size. It also can result from a noninferiority margin that is too wide. E and F, If the CI includes Δ and zero, the difference is nonsignificant but the result regarding noninferiority is inconclusive. G, If the CI includes Δ and is wholly to the right of zero, the difference is statistically significant but the result is inconclusive regarding possible inferiority of magnitude Δ or worse. H, If the CI is wholly above Δ, the new treatment is inferior.
[a] This CI indicates noninferiority in the sense that it does not include Δ, but the new treatment is significantly worse than the standard. Such a result is unlikely because it would require a very large sample size.
[b] This CI is inconclusive in that it is still plausible that the true treatment difference is less than Δ, but the new treatment is significantly worse than the standard. Adapted from Piaggio et al.[6]

As we will not have knowledge of treatment group assignment (whether Group A or Group B is our "new treatment", here, no irrigation), and to preserve our blinding, we have deemed it necessary to take both scenarios under consideration, as follows:

- We will calculate the treatment group difference assuming first that Group A is the "new treatment" and then that Group B is the "new treatment" (Scenario 1 and Scenario 2).
- We will plot the resulting point estimate with confidence intervals (97.5% CIs) into two separate graphs.
- We will interpret both graphs (Figures 2 and 3).

Figure 2. Scenario 1 – Group A minus Group B.

[*EXAMPLE GRAPH BELOW*, to be replaced by the actual graph of the FINISH trial data]

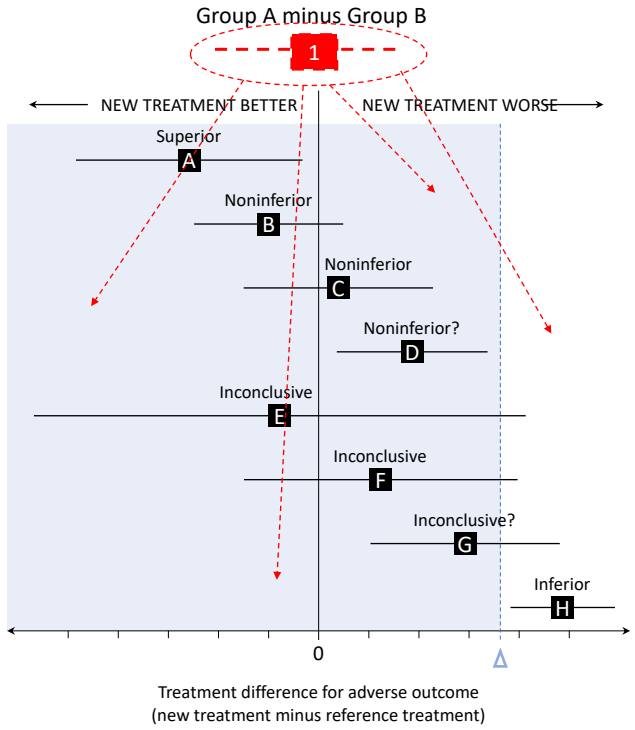
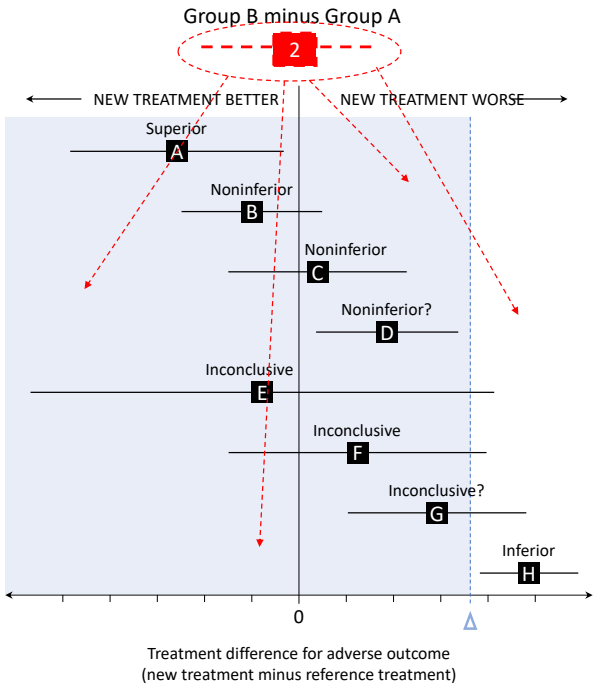


Figure 3. Scenario 2 – Group B minus Group A.

[*EXAMPLE GRAPH BELOW*, to be replaced by the actual graph of the FINISH trial data]



Step 2: Initial interpretation of efficacy

Based on the location of the whole CI in relation to Δ (non-inferiority margin), our initial interpretation on the non-inferiority of no irrigation vs. irrigation, is as follows:

Scenario 1 (Figure 2) [*INCORRECT OPTION TO BE REMOVED*]

1. Among adults with symptomatic chronic subdural hematoma who had undergone burr-hole drainage, Group A was [superior A / non-inferior B, C, D / inferior H] to Group B in preventing reoperations.

OR

2. Among adults with symptomatic chronic subdural hematoma who had undergone burr-hole drainage, the effect of Group A compared to Group B in preventing reoperations was inconclusive [E, F, G].

Scenario 2 (Figure 3) [*INCORRECT OPTION TO BE REMOVED*]

3. Among adults with symptomatic chronic subdural hematoma who had undergone burr-hole drainage, Group B was [superior A / non-inferior B, C, D / inferior H] to Group A in preventing reoperations.

OR

4. Among adults with symptomatic chronic subdural hematoma who had undergone burr-hole drainage, the effect of Group A compared to Group B in preventing reoperations was inconclusive [E, F, G].

Step 3: Analysis of safety concerns

Given that the objective of surgery for CSDH extends beyond preventing reoperations to also encompass the improvement of neurological function and prevention of death, the entire treatment effect of intraoperative irrigation (versus no irrigation) may not be adequately captured by focusing solely on the primary outcome measure, the rate of reoperations. We deemed it crucial to also consider the potential impact of between-group differences in deaths and/or unfavorable functional outcomes, as both could have an effect on the rate of reoperations. We felt that in the name of transparency and trustworthiness, we would need to define *a priori* thresholds for between-group differences in mortality and rate of unfavorable functional outcome (mRS 4–6) at 6-months that we consider "concerning" or "alarming".

We considered a difference to be "concerning" if the 85% confidence interval (CI) of the absolute between-group difference in mortality or rates of unfavorable functional outcome (mRS 4-6) did not encompass the value of 0.0 and "alarming" if the 95% CI of the absolute between-group difference in mortality or mRS 4-6 rates did not encompass the value of 0.0.

Prior to establishing the thresholds for the 85% CI ("concerning") and 95% CI ("alarming") thresholds, we conducted simulations to ensure that these thresholds would yield clinically relevant differences in mortality and unfavorable functional outcome (mRS 4-6) (Figure 4). For the mortality simulations, we assumed a mortality rate of 5% in the standard care group. This selection was based on two recent similar-sized RCTs, in similar settings (Sweden [11], UK [12]), where the 6-month mortality rate was 5% in the groups treated with burr-hole craniostomy and subdural drainage. As for the mRS 4–6 simulations, we assumed an mRS 4–6 rate of 10% based on the results of the DEX-CSDH [12] and DESCA trials [13].

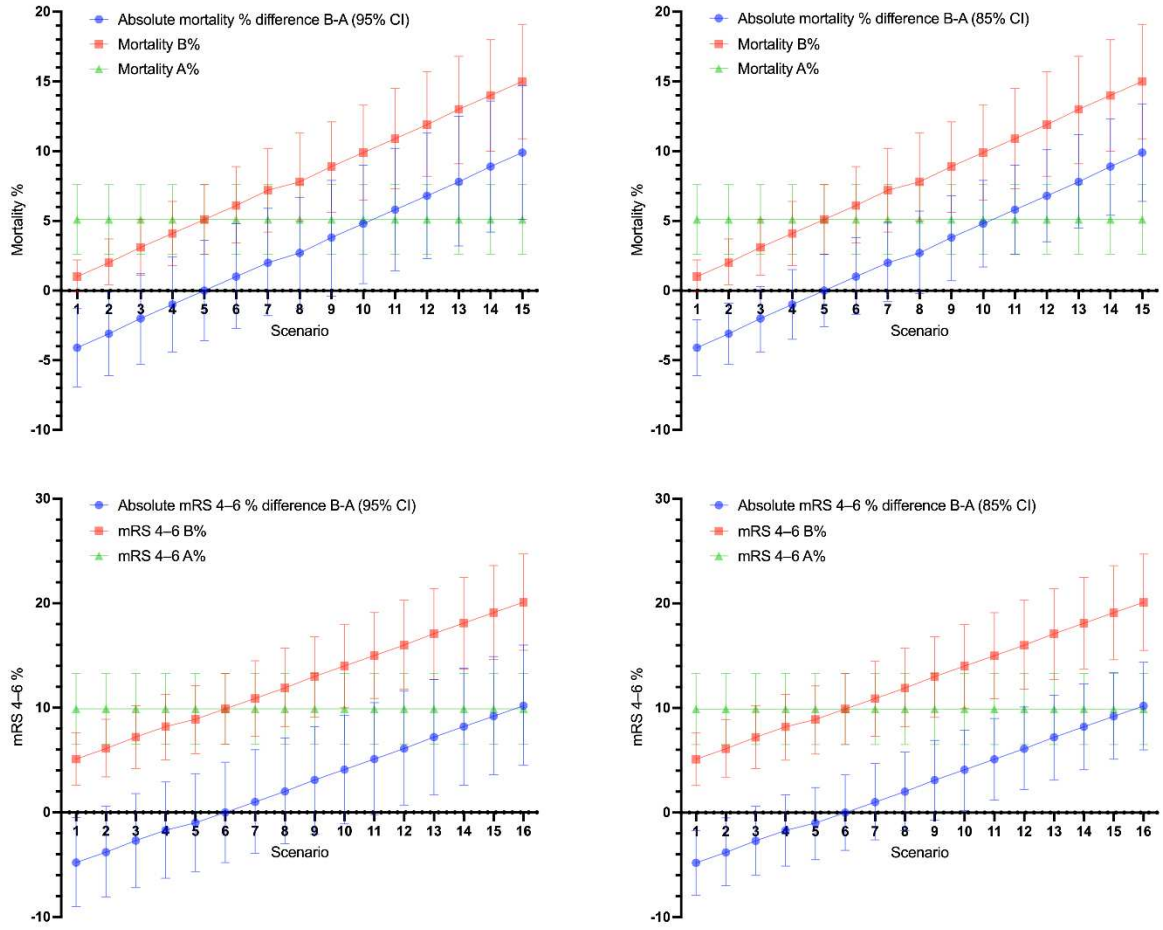


Figure 4. Simulation of the 95% (left panel) and 85% (right panel) confidence intervals for between-group differences in 6-month mortality rates (upper panel) and rates of mRS 4–6 (lower panel). The difference in mortality and/or rates of mRS 4–6 is significant if the 85% CI or 95% CI does not encompass the value of 0.0.

Acknowledging that the FINISH trial was not powered for assessing differences in mortality or rate of unfavorable functional outcome (mRS 4–6), we used a 3-level hierarchy (**low** / **moderate** / **high**) for expressing our confidence in the possible between-group differences according to the GRADE approach [14–16]. We assumed a 6-month mortality rate of 5% [12,17] and an mRS 4–6 rate of 10% [12]. In terms of **mortality**, the confidence in the estimate was considered **low** if the overall 6-month mortality rate was **<5%**, **moderate** if the overall 6-month mortality rate was **5–10%**, and **high** if the overall 6-month mortality rate was **>10%**. Regarding 6-month unfavorable functional outcome (**mRS 4–6**), the confidence in the estimate was considered **low** if the rate of mRS 4–6 was **<10%**, **moderate** if the rate of mRS 4–6 was **10–15%**, and **high** if the rate of mRS 4–6 was **>15%**.

Our scheme for interpreting the possible safety concerns is outlined in Tables 3 and 4.

Table 3. A priori set thresholds for **concerning** and **alarming** between-group differences in 6-month mortality with associated confidence estimates and pre-determined commitments for interpretation.

Overall mortality in whole population	Confidence in estimate	Threshold for relevant between-group difference in mortality	Resulting action if threshold fulfilled	Authors' interpretation commitment
<5%	Low	**Concerning**: The 85% confidence interval of the between-group difference in absolute mortality-% does not include 0.0	None	We refrain from making any comments due to the low event rate (low confidence in effect estimate).
		Alarming: The 95% confidence interval of the between-group difference in absolute mortality-% does not include 0.0	Notion on safety concern added to the discussion (not added to the conclusion).	Group A/B was associated with an **alarmingly** higher mortality rate. Given the event rate, the confidence in this finding was **low**.
5-10%	Moderate	**Concerning**: The 85% confidence interval of the between-group difference in absolute mortality-% does not include 0.0	Notion on safety concern added to the discussion (not added to the conclusion).	Group A/B was associated with a **concerningly** higher mortality rate. Given the event rate, the confidence in this finding was **moderate**.
		Alarming: The 95% confidence interval of the between-group difference in absolute mortality-% does not include 0.0	Notion on safety concern added to the conclusion.	Group A/B was associated with an **alarmingly** higher mortality rate. Given the event rate, the confidence in this finding was **moderate**.
>10%	High	**Concerning**: The 85% confidence interval of the between-group difference in absolute mortality-% does not include 0.0	Notion on safety concern added to the conclusion.	Group A/B was associated with a **concerningly** higher mortality rate. Given the event rate, the confidence in this finding was **high**.
		Alarming: The 95% confidence interval of the between-group difference in absolute mortality-% does not include 0.0	Notion on safety concern added to the conclusion.	Group A/B was associated with an **alarmingly** higher mortality rate. Given the event rate, the confidence in this finding was **high**.

Table 4: A priori set thresholds for concerning and alarming between-group differences in 6-month mRS4−6 with associated confidence estimates and pre-determined commitments for interpretation

Overall mRS 4-6 in whole population	Confidence in estimate	Threshold for relevant between-group difference in mRS 4–6	Resulting action if threshold fulfilled	Authors' interpretation commitment
<10%	Low	**Concerning**: The 85% confidence interval of the between-group difference in absolute mRS 4–6 rate does not include 0.0	None	We refrain from making any comments due to the low event rate (low confidence in effect estimate).
		Alarming: The 95% confidence interval of the between-group difference in absolute mRS 4–6 rate does not include 0.0	Notion on safety concern added to the discussion (not added to the conclusion).	Group A/B was associated with an **alarmingly** higher rate of unfavorable functional outcome. Given the event rate, the confidence in this finding was **low**.
10-15%	Moderate	**Concerning**: The 85% confidence interval of the between-group difference in absolute mRS 4–6 rate does not include 0.0	Notion on safety concern added to the discussion (not added to the conclusion).	Group A/B was associated with a **concerningly** higher rate of unfavorable functional outcome. Given the event rate, the confidence in this finding was **moderate**.
		Alarming: The 95% confidence interval of the between-group difference in absolute mRS 4–6 rate does not include 0.0	Notion on safety concern added to the conclusion.	Group A/B was associated with an **alarmingly** higher rate of unfavorable functional outcome. Given the event rate, the confidence in this finding was **moderate**.
>15%	High	**Concerning**: The 85% confidence interval of the between-group difference in absolute mRS 4–6 rate does not include 0.0	Notion on safety concern added to the conclusion.	Group A/B was associated with a **concerningly** higher rate of unfavorable functional outcome. Given the event rate, the confidence in this finding was **high**.
		Alarming: The 95% confidence interval of the between-group difference in absolute mRS 4–6 rate does not include 0.0	Notion on safety concern added to the conclusion.	Group A/B was associated with an **alarmingly** higher rate of unfavorable functional outcome. Given the event rate, the confidence in this finding was **high**.

Table 5. Safety concerns for the intention-to-treat dataset.

Variable	All patients (n=??)	Group A (n=??)	Group B (n=??)	Difference (95% CI)	Difference (85% CI)	P-value
6 mo mortality	??/n (??%)	??/n (??%)	??/n (??%)	x (x to x)	x (x to x)	??
6 mo mRS 4–6	??/n (??%)	??/n (??%)	??/n (??%)	x (x to x)	x (x to x)	??

Abbreviations: mRS=modified Ranking Scale, CI=confidence interval

Table 6. Safety concerns for the per-protocol dataset.

Variable	All patients (n=??)	Group A (n=??)	Group B (n=??)	Difference (95% CI)	Difference (85% CI)	P-value
6 mo mortality	??/n (??%)	??/n (??%)	??/n (??%)	x (x to x)	x (x to x)	??
6 mo mRS 4–6	??/n (??%)	??/n (??%)	??/n (??%)	x (x to x)	x (x to x)	??

Abbreviations: mRS=modified Ranking Scale, CI=confidence interval

Imbalance in the incidence of safety concerns (mortality and/or mRS 4–6)?

NO / YES [*INCORRECT OPTION TO BE REMOVED*]

If NO, the following sentence will be added to the conclusion: “There were no relevant differences in mortality or functional outcome between the groups.”

If YES, interpretation according to **Table 3** (mortality) and **Table 4** (unfavorable functional outcome)

Step 4: Unblinding of treatment groups

Having now considered both the rate of reoperations and safety concerns, we have now reached a consensus on our blinded assessment of efficacy.

Our statistician will now unblind the treatment group assignment (break the randomization code):

- Group A = Irrigation / No irrigation [*INCORRECT OPTION TO BE REMOVED*]
- Group B = Irrigation / No irrigation [*INCORRECT OPTION TO BE REMOVED*]

Given the above noted, the FINISH data is shown in **Table 1**, **Table 2, Table 5 and Table 6** (with n-values for Groups to be added) and in Scenario 1 (**Figure 2**) or Scenario 2 (**Figure 3**). [*INCORRECT OPTION TO BE REMOVED*]. The rate of crossovers is reported here:

- Crossovers from Group A to B, n=*??* *[INSERT DATA]*
- Crossovers from Group B to A, n=*??* *[INSERT DATA]*

[*COPY TABLE 1 HERE AND INSERT DATA*]

[*COPY TABLE 2 HERE AND INSERT DATA*]

[*COPY TABLE 5 HERE AND INSERT DATA*]

[*COPY TABLE 6 HERE AND INSERT DATA*]

[*COPY FIGURE 2 OR FIGURE 3 HERE*]

Step 5: Unblinded interpretation of treatment effect

Accordingly, our penultimate interpretation of the FINISH trial is as follows:

[*CORRECT OPTION TO BE CHOSEN*]

Treatment comparison	**Primary outcome results**	**Interpretation based on primary outcome**	**Between-group difference in safety concerns (mortality, mRS 4-6)**	**Interpretation commitment regarding safety concerns (mortality, mRS 4-6)**
No intraoperative irrigation vs. intraoperative irrigation	Non-inferior	Among adults with symptomatic chronic subdural hematoma who had undergone burr-hole drainage, no intraoperative irrigation was **noninferior** to intraoperative irrigation in preventing reoperations.	No difference	There were no relevant differences in mortality or functional outcome between the groups.
			Difference	"*Interpretation commitment*" from Tables 3 and 4 added if criteria for addition to conclusion is fulfilled.
	Superior	Among adults with symptomatic chronic subdural hematoma who had undergone burr-hole drainage, no intraoperative irrigation was **superior** to intraoperative irrigation in preventing reoperations. However, be it noted that we did not design the study to show superiority.	No difference	There were no relevant differences in mortality or functional outcome between the groups.
			Difference	"*Interpretation commitment*" from Tables 3 and 4 added if criteria for addition to conclusion is fulfilled.
	Inferior	Among adults with symptomatic chronic subdural hematoma who had undergone burr-hole drainage, no intraoperative irrigation was **inferior** to intraoperative irrigation in preventing reoperations. However, be it noted that we did not design the study to show inferiority.	No difference	There were no relevant differences in mortality or functional outcome between the groups.
			Difference	"*Interpretation commitment*" from Tables 3 and 4 added if criteria for addition to conclusion is fulfilled.
	Inconclusive	Among adults with symptomatic chronic subdural hematoma who had undergone burr-hole drainage, the effect of intraoperative irrigation compared to no intraoperative irrigation in preventing reoperations was **inconclusive**.	No difference	There were no relevant differences in mortality or functional outcome between the groups.
			Difference	"*Interpretation commitment*" from Tables 3 and 4 added if criteria for addition to conclusion is fulfilled.

Step 6: Final interpretation

Our final interpretation of the FINISH trial stands as follows:

[*COPY PASTE THE CORRECT INTERPRETATION HERE FROM STEP 5*]

Place: [*ZOOM-/Teams-meeting*]
Time: [*Insert date here*]

Teppo LN Järvinen (BDI committee chair)	Simo Taimela (BDI committee co-chair)	Tomasz Czuba (trial statistician)
_____	_____	_____
Riku Kivisaari (BDI committee member)	Christoph Schwartz, member (BDI committee member)	
_____	_____	

Also present at the meeting:

4. References

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