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COVeRs to impRove EsthetiC ouTcome after Surgery for Chronic subdural hemAtoma by buRr hole trepanation (CORRECT-SCAR) – protocol of a single-blinded, randomized controlled trial

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Keywords:	Chronic subdural hematoma, Esthetic outcome, Patient satisfaction, Burr hole cover, Trepanation, Value-based medicine

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Manuscripts

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3 1 **COVeRs to impRove EsthetiC ouTcome after Surgery for Chronic subdural hemAtoma**
4 **by buRr hole trepanation (CORRECT-SCAR) – protocol of a single-blinded,**
5 **2 randomized controlled trial**
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13 8 MD/PhD; **on behalf of the CORRECT-SCAR study group***
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53 27 **Previous presentations:**

54 28 None.
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30 **Appendix: Contributors of the “CORRECT-SCAR study group” (persons listed in**
31 **alphabetical order):**

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- 2 – Jorn Fierstra, MD/PhD
- 3 – Dilek Könü-Leblebicioglu, MD
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- 8 – Lennart H. Stieglitz, MD

For peer review only

1 **Abstract**

2 **Introduction:** Outcomes rated on impairment scales are satisfactory after burr hole
3 trepanation for chronic subdural hematoma (cSDH). However, the surgery leads to bony
4 defects in the skull with skin depressions above that are frequently considered esthetically
5 unsatisfactory by patients. Those defects could be covered by approved medical devices (burr
6 hole covers), but this is rarely done today. We wish to assess, whether the application of burr
7 hole covers after trepanation for the evacuation of cSDH leads to higher patient satisfaction
8 with the esthetical result at 90 days postoperative, without worsening disability outcomes or
9 increasing the complication rate.

10 **Methods and analysis:** This is a prospective, single-blinded, randomized, controlled,
11 investigator initiated clinical trial enrolling eighty adult patients with first-time uni- or
12 bilateral cSDH. The primary outcome is the difference in satisfaction with the esthetic result
13 of the scar, comparing patients allocated to the intervention (burr hole cover) and control (no
14 burr hole cover) group, measured on the Aesthetic Numeric Analogue scale at 90 days
15 postoperative. Secondary outcomes include differences in the rates of skin depression,
16 complications, as well as neurological, disability and health-related quality of life outcomes
17 until 12 months postoperative.

18 **Ethics and dissemination:** The institutional review board approved this study on January
19 29th 2019 under case number BASEC 2018-01180. This study determines, whether a
20 relatively minor modification of a standard surgical procedure can improve patient
21 satisfaction, without worsening functional outcomes or increasing the complication rate. The
22 outcome corresponds to the value-based medicine approach of modern patient-centered
23 medicine.

24 **Trial registration:** ClinicalTrials.gov identifier: NCT03755349.

25 **Key words**

26 Burr hole cover; Chronic subdural hematoma; Trepanation; Esthetic outcome; Complications;
27 Scar; Patient satisfaction; Burr hole plate

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2
3 **1 Article summary – strengths and limitations of this study**
4

- 5 2 - The study might prove that surgeons can positively influence the satisfaction of their
6 3 patients by a minor and inexpensive technical nuance (adding a burr hole cover before
7 4 skin closure).
8
9 5 - By randomizing patients with unilateral cSDH into an intervention and control group,
10 6 the effect of potential confounders should be minimized.
11
12 7 - The inclusion of patients with bilateral cSDH allows studying a completely unbiased
13 8 effect of burr hole covers on the outcome of interest (as each patient serves as his/her
14 9 own internal control).
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16 10 - The 90-day period of the primary endpoint may be too short to detect a difference in
17 11 outcome (as skin depressions progressively occur over time), but additional 12-month
18 12 outcome assessment should capture this.
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1 **General Information**

2 Protocol title: COVeRs to impROve EsthetiC ouTcome after Surgery for Chronic subdural
3 hemAtoma by buRr hole trepanation (CORRECT-SCAR) - a single-blinded, randomized
4 controlled trial

5
6 Protocol identifying number: BASEC 2018-01180

7
8 Date of acceptance by institutional review board: January 29th 2019

9
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1 Introduction

2 Outcome in terms of recovery of impaired neurological function is generally satisfactory after
3 burr hole trepanation for the evacuation of chronic subdural hematoma (cSDH).[1 2] Despite
4 being considered a relative minimally invasive type of surgery, it requires drilling holes in the
5 patient's skull. With progressive hematoma reabsorption during follow-up, patients may
6 develop skin depressions above the burr hole sites (Figure 1).[3 4] Theoretically, burr holes
7 could be covered by approved medical devices (burr hole covers) after cSDH evacuation and
8 prior to closing the wound.

9 This has not become standard of care, however, and we previously set out to explore
10 the prevalence and relevance of skin depressions, as well as today's pattern of care by
11 conducting a cross-sectional survey-based study among neurosurgeons globally. Analyzing
12 576 responses from 78 different countries, 76% of neurosurgeons stated that their patients
13 complained about skin depressions after burr hole trepanations more or less frequently. In
14 contrary, only 28% of neurosurgeons currently apply burr hole covers more or less frequently
15 for this indication. Their reluctance was mostly explained by a lack of evidence for any
16 proven benefit, less so for the fear of an increased complication rate, technical difficulties and
17 financial reasons. Around three quarters (78% of neurosurgeons) indicated that they would
18 consider applying burr hole covers for this indication, in case a high-quality trial
19 demonstrated its efficacy and safety (unpublished data, April 2019).

20 We retrospectively reviewed a series of n=28 cSDH patients (64 burr holes) treated at
21 our department, of which n=11 patients had received a burr hole cover on 14 burr holes at the
22 surgeon's discretion. Applying the Aesthetic Numeric Analogue (ANA) scale to rate the
23 esthetical result of the surgery,[5] patients rated sites where the burr hole was covered more
24 favorably than sites where the burr hole was left uncovered (ANA 9.3±0.74 vs. 7.9±1.0;
25 p<0.001).[4] In addition, the rates of skin depression were as low as 7% in the intervention
26 group and as high as 92% in the control group (p<0.001). Evidently, the prior results were
27 subject to selection bias, patients were not blinded for the intervention and the study was
28 underpowered to estimate possible group differences in complications.[4] These preliminary
29 findings were a promising starting point for further and more in-depth research, because
30 filling this knowledge gap is likely to affect future management of cSDH patients.

32 Methods and analysis

33 *Study Goals and Objectives*

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3 1 The CORRECT SCAR trial aims to demonstrate that the placement of burr hole covers on the
4 burr hole sites improves patient satisfaction with the esthetic outcome of the surgical
5 2 procedure at 3 and 12 months postoperative. It also aims to demonstrate that clinical
6 3 outcomes (disability, neurological function & health-related quality of life (hrQoL)) remain
7 4 similar and complication rates (e.g., surgical site infections (SSIs), cSDH recurrences, etc.)
8 5 are not increased by applying burr hole covers.
9 6

10 7 The primary objective is to compare mean ANA scores (patient satisfaction with the
11 8 esthetic result of the surgery) between the intervention and control group at 90 days
12 9 postoperatively. Secondary/safety objectives are to compare mean ANA scores, rates of skin
13 10 depression, impairment in activities of daily living (ADLs), disability (modified Rankin scale
14 11 (mRS)), hrQoL (Euro-Qol (EQ)-5D), neurological status (National Institute of Health Stroke
15 12 scale (NIHSS)), complications and residual hematoma volume between the intervention and
16 13 control group at 3 and 12 months postoperative.
17 14

15 *Study Design*

16 16 Prospective, single-blinded, randomized, controlled, investigator initiated clinical trial. The
17 17 trial is conducted at the University Hospital Zurich, Switzerland. The study will be reported
18 18 according to the CONSORT guidelines.[6]

19 *Eligibility criteria*

20 20 Participants fulfilling all of the following inclusion criteria are eligible for the study:

- 21 21 - Patients with first-time cSDH (hypodense, isodense, hyperdense or mixed-type in CT-
22 22 imaging), scheduled for uni- or bilateral double burr hole trepanation under general
23 23 anesthesia
- 24 24 - Patient age \geq 18 years
- 25 25 - Patient non-comatose at time of inclusion (GCS > 8 points)
- 26 26 - Patient able to communicate (in terms of ability to hear, see, speak and understand).

27
28 28 The presence of any one of the following exclusion criteria will lead to exclusion of the
29 29 participant:

- 30 30 - Patient with recurrent cSDH or previous surgery for cSDH
- 31 31 - Patient with cSDH treated by craniotomy or by single burr hole trepanation
- 32 32 - Patient with cSDH treated in local anesthesia
- 33 33 - Patient unlikely to attend the follow-up (due to reasons of residency, dismal prognosis,
34 34 etc.)

- 1 - Pregnancy
- 2 - Known allergy against or incompatibility with Titanium
- 3 - Known or suspected non-compliance
- 4 - Inability to follow the study procedures, e.g. due to psychological disorders, dementia, etc. of the participant.

6 *Intervention & study groups*

7 A study algorithm can be found in figure 2 and table 1 outlines all visits and procedures.

8 1. Patients with unilateral cSDH

9 All patients randomized into the control group will be treated according to our
10 standard protocol for cSDH evacuation (supplementary digital content 1).

11 All patients randomized into the intervention group will be treated according to our
12 standard protocol for cSDH evacuation with one exception: placement of a burr hole
13 cover (UN3 BURR HOLE COVER, 20mm, W/TAB, Item code 53-34520, Stryker®,
14 Kalamazoo, Michigan) that is fixed with 2 screws (UNIII AXS SCREWS, SELF-
15 DRILLING, 1.5 x 4MM, Item code 56-15934, Stryker®, Kalamazoo, Michigan) on
16 both burr holes after evacuation of the hematoma and prior to skin closure.

17 2. Patients with bilateral cSDH

18 Patients with bilateral cSDH serve as their own internal control. They are randomized
19 concerning the intervention or control side, being either the side with larger or smaller
20 hematoma, respectively.

21 All patients are blinded concerning the study group/side allocation. For application of the burr
22 hole cover, surgeons will be instructed to firmly press the burr hole cover on the burr hole
23 before receiving the screws from the scrub nurse in order to prevent from screws accidentally
24 falling into the subdural space. For this purpose, a standard operating procedure (SOP) has
25 been developed (supplementary digital content 2).

26 *Primary Outcome and Follow-Up*

27 For the primary outcome, patient satisfaction with the esthetic results of the scar is determined
28 using a patient-rated outcome measure (PROM), the ANA scale,[5] ranging from 0
29 (dissatisfied) – 10 (very satisfied), at 90 days postoperative. The outcome is assessed by
30 mailed questionnaire and collected by a study coordinator.

31 *Secondary Outcomes*

- 32 - Patient satisfaction with the esthetic result of the scar, determined by the ANA scale,
33 at 12 months postoperatively (mailed questionnaire, collected by a study coordinator).

- 1 - Impairment in ADLs (e.g., when hairdressing, combing, washing, etc.), rated as “yes” vs. “no”, at 90 days and 12 months postoperative (mailed questionnaire, collected by a study coordinator).
- 2 - Rate of skin depression, rated as “yes” vs. “no”, at 90 days and 12 months postoperative (mailed questionnaire, collected by a study coordinator).
- 3 - Disability, determined by the mRS (ranging from 0 (no disability) to 6 (dead)) at 90 days.
- 4 - HrQoL, determined by the EQ-5D (allowing the calculation of both the EQ-5D index that ranges from -0.074 (worst hrQoL) – 1.00 (best hrQoL) using European norms and the EQ-5D VAS (ranging from 0 (worst hrQoL) – 100 mm (best hrQoL)), at 90 days and 12 months postoperative (mailed questionnaire, collected by a study coordinator).
- 5 - Neurological outcome, determined by the NIHSS (ranging from 0 (no neurological deficit) – 42 (severe neurological deficit)), at 90 days.
- 6 - Home time, as surrogate marker of disability,[7] at 90 days and 12 months.

Further safety-outcomes are assessed:

- 7 - Intra- and postoperative complications up to 90 days and 12 months, in particular cSDH recurrence and SSIs.
- 8 - Residual cSDH volume in ccm^3 , absolute (ccm^3) and relative (%) cSDH clearance at 90 days postoperative (measured by two neuroradiologists independently, otherwise not involved in the project, using volumetric analysis).

Patient and Public Involvement

Other than recruiting patients admitted to our hospital, it is not intended to involve patients and the public in the design, conduct and reporting of this research.

Ethics and dissemination

Despite the generally favorable risk profile and outcome of burr hole trepanation for cSDH, skin depressions may occur weeks and months after hematoma reabsorption.[3 4] These are frequently considered esthetically unsatisfactory by patients and may lead to functional restrictions, e.g. when combing, hairdressing or washing. In own clinical experience, patients reported being stared-at for these skin depressions, evoking feelings of astonishment and aversion from both family members and strangers. With an increasing number of senior citizens in good physical/mental health and leading active social lives, the esthetic aspect of

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3 1 outcome gains new importance. Today's elderly patients do no longer content themselves
4 with a basic surgical procedure, but – as informed customers – expect optimal surgical results
5 2 topped with an excellent service.[8]
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8 4 In theory, burr hole covers represent an effective, easy-to-apply and relatively
9 inexpensive solution to prevent cosmetically and functionally unfavorable skin
10 5 depressions.[4] Our survey has clearly demonstrated that – in order to improve the acceptance
11 6 of this technical nuance – its efficiency needs to be demonstrated first (unpublished data,
12 7 April 2019). Moreover, as the intervention is unlikely to improve any “hard outcome” such as
13 8 disability or survival, more data should substantiate its safety.
14 9

15 10 We consider a prospective, randomized, blinded and controlled study design optimal
16 11 to prove a causal relationship between the study intervention and outcome. A clear strength of
17 12 this study is that patients with bilateral cSDH can be included and serve as their own internal
18 13 controls. Any retrospective approach to the study question, or applying the burr hole cover in
19 14 a prospective fashion and comparing it to a (historical) control group is not possible, as the
20 15 outcome of interest (ANA scale) has not been established in patients before, as well as for the
21 16 likelihood of selection bias. The study aim corresponds to the value-based medicine approach
22 17 of modern patient-centered medicine.
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33 18 *Trial Status*

34 19 The study has started enrolling patients on January 29th 2019.
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38 21 *Safety Considerations*

39 22 Burr hole covers are applied according to a SOP (supplementary digital content 2) and the
40 23 medical device is approved for the studied application. All device deficiencies, (severe)
41 24 adverse events ((S)AEs) and (severe) adverse device effects ((S)ADEs) are systematically
42 25 recorded. The Clinical Trials Center (CTC) of the University of Zurich externally monitors
43 26 the trial.
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50 27 *Follow-up*

51 28 Participating patients are followed up to 12 months postoperative.
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55 30 *Unblinding*

56 31 Maintenance of trial treatment randomization codes will be done by the electronic data
57 32 capturing system (run by the CTC Zurich), using a built-in tool for randomization. Breaking
58 33 codes is not allowed. Unblinding (and revealing a participant's allocated intervention)
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3 1 towards the patient is permissible only if the trial is suspended, prematurely terminated due to
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5 2 security concerns or completed.
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8 4 *Data Managements and Statistical Analysis*

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10 5 The data is hosted by the CTC, University of Zurich. Electronic case report forms (eCRFs)
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12 6 are implemented. All data are stored on a server in a dedicated database. A role concept with
13
14 7 personal passwords (site investigator, statistician, monitor, administrator etc.) regulates
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16 8 permission.

17 9 *Handling of missing data*

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20 10 First, the risk of missing data will be minimized by regular data reviews, also with an
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22 11 intention to identify at risk patients for lack of follow-up data. Even though the effect of skin
23
24 12 depression is likely more pronounced at 12 months, compared to 90 days postoperative, we
25
26 13 intentionally chose to select the 90-day time point as primary outcome in order to minimize
27
28 14 drop-out. Contingency plans foresee home/rehabilitation visits by study personnel to obtain
29
30 15 otherwise missing data in patients who cannot show up for the planned 90-day or 12-month
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32 16 follow-up.[9] Patients who die during the study interval (or cannot be evaluated as aphasic or
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34 17 in too poor clinical condition) and in whom for this reason the primary endpoint cannot be
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36 18 obtained will be recorded as not assessable for the primary outcome. Sensitivity analyses will
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38 19 be performed for this study.

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20 If, despite the above-mentioned mechanisms, missing data is present we use the
21 following protocol: First, mechanisms of missing data are assessed. If the data are deemed
22 missing at random, and there is <10-15% of patients with time point missing data, then case
23 deletion will be used (and additional patients will be recruited). Second, if the missing data
24 mechanism is not at random, multiple imputation will be performed, a well-accepted method
25 for intention to treat analysis in RCT with missing outcome data.[9 10]

26 26 *Determination of sample size*

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27 Based on an expected mean satisfaction score of 9/10 on the ANA in the intervention and
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29 7/10 on the ANA in the control group, n=37 patients need to be randomized in each study arm
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31 in order to find a statistically significant difference in the primary outcome with alpha set at
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33 0.05, a power of 80% and an estimated standard deviation of 3.[4] Based on a total sample
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35 size of $2 \times 37 = 74$, with an estimated dropout rate of 10%, we plan to include n=80 patients in
36
37 total.

1 *Methods used to minimize bias*

2 A computerized randomization tool, provided by the electronic data capturing system, is used
3 with the only strata being uni- or bilateral cSDH. The random allocation sequence is
4 generated by the CTC, University of Zurich. Study physicians conduct patient enrollment and
5 randomization after basic patient data has been entered into eCRFs. Due to the randomization
6 process, patients with unilateral cSDH are likely to be well balanced for most important
7 parameters that could potentially influence the primary outcome. In patients with bilateral
8 cSDH, each patient serves as his/her own control, which minimizes the risk of bias (=setting
9 of a n-of-1 clinical trial).[11]

10 Patients with unilateral cSDH will be randomized in a 1:1 fashion into the intervention
11 or control group, respectively. Patients with bilateral cSDH will be randomized in a 1:1
12 fashion concerning the intervention side, being either the side with more or lesser hematoma
13 size (Figure 2).

14 Patients will be blinded for allocation to the study group/side, but surgeons will not be.
15 Patients will not be aware of the study group/side, since the operation takes place under
16 general anesthesia. The fact that patients are blinded for the study group allocation will be
17 mentioned in the discharge letter (in order to inform the family physician), and the
18 neurosurgical team of nurses and physicians will also be informed not to “unblind” the patient.

19 The primary endpoint and most of the secondary endpoints will be determined by
20 mailed questionnaires. This way, the patient will not be influenced by the presence of the
21 physician when judging on satisfaction with the esthetical result of the surgery. In addition,
22 all data is collected by a dedicated study coordinator (E.J.), who is not involved in the patient
23 care (=independent outcome assessment).

24 *Primary analysis*

25 The main analysis will be according to the intention to treat (ITT) protocol. An as-treated
26 analysis will be performed, additionally.

27 Satisfaction on the ANA scale for both the frontal and parietal scar are measured
28 separately, but a mean satisfaction score is built by adding the values and dividing the sum by
29 two. For analysis of the primary outcome the results obtained in the intervention group
30 (unilateral cSDH) and on the intervention side (bilateral cSDH) will be combined and
31 compared to the combined results obtained in the control group and on the control side. As
32 the dependent variable is a quantitative variable on an interval scale, a rank-sum test is
33 appropriate to analyze group differences. Even though no formal minimum clinically
34 important difference (MCID) of the ANA-scale has been determined, we powered the study to

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3 1 detect an in-between group difference in outcome of two points, as – abstracted from the
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5 2 numeric rating scale for pain (also ranging between 0 – 10) – a change of two points is
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7 3 considered to be well above the MCID,[12] therefore resulting in a clinically meaningful
8
9 4 improvement for the patient.

10 5 Subgroup analyses will be made for patients with bald heads vs. patients with scalp
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12 6 hair, male vs. female patients, patients < 60 years vs. ≥ 60 years and for patients with bilateral
13
14 7 cSDH.

15 16 8 *Secondary analyses*

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18 9 As the remaining secondary outcomes are not side-specific but reflect the condition of the
19
20 10 patient as a whole, the remaining secondary analyses will compare results obtained in patients
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22 11 with unilateral cSDH randomized into either the intervention or control group.

23 12 As the safety outcomes are specific for the incision site and side, for the safety
24
25 13 analyses the results obtained in the intervention group and on the intervention side will be
26
27 14 combined and compared to the combined results obtained in the control group and on the
28
29 15 controlled side.

30 16 For the outcomes that are quantitative (hrQoL on the EQ-5D) student's t-tests or rank-
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32 17 sum tests will be applied, depending on normally distributed data or not. For the outcomes
33
34 18 that are categorical (type of impairment with ADLs, disability on the mRS, neurological
35
36 19 outcome on the NIHSS, complications on the CDG) descriptive analyses and chi-square tests
37
38 20 will be applied. For the outcomes that are binary (impairment with ADLs, skin depression,
39
40 21 etc.) logistic regression analysis will be performed, calculating the odds ratio (OR) and 95%
41
42 22 confidence intervals (CIs).

43 23 *Interim analyses*

44
45 24 Once data of 50 patients with completed 90-day follow-up data has been collected, the
46
47 25 primary endpoint and the safety analyses will be performed.

48 49 50 27 *Quality Assurance*

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52 28 The study is conducted in accordance with good clinical practice (GCP) guidelines. All source
53
54 29 data is accessible for monitoring, audits and inspections. Authorities have the right to perform
55
56 30 inspections and on-site auditing. External monitoring will be performed by the CTC,
57
58 31 University of Zurich, as detailed in a monitoring plan including pre-study, site initiation,
59
60 32 routine monitoring and close-out visits, considering local infrastructure, completeness of

1 documents, patient safety, adherence to the study protocol, data quality entered into the
2 eCRFs and the trial master file.

3 Progress of patient inclusion and data completeness is continuously (at least once
4 every two weeks) checked by a study coordinator (E.J.).

5 *Expected Outcomes of the Study*

6 The study will shed more light on the question, whether patient satisfaction with the esthetic
7 result of the surgical procedure can be improved by adding burr hole covers on the burr holes
8 after trepanation for cSDH. An improvement in patient satisfaction would likely be conferred
9 through the decreased prevalence of skin depressions, as a strong difference in prevalence of
10 skin depressions was previously found in two retrospective studies.[3 4] The study will
11 moreover allow to understand better, whether the application of burr hole covers increases the
12 risks of complications, e.g. cSDH recurrence or SSIs. Results of the study are likely to affect
13 future management of cSDH patients.

14 *Duration of the project*

15 Recruitment is expected to be completed by the end of January 2021, with final follow-up
16 collected until January 2022. Publication of the final results is expected around six months
17 after last patient out.

18 *Project management*

19 The principle investigators (M.N.S. & M.R.G.) are responsible for patient inclusion, quality
20 of data collection and adhesion to the protocol. They are supported by a team of site
21 investigators, a dedicated study coordinator (E.J.), the monitoring staff and the sponsor (L.R.).

22 *Ethics*

23 The study protocol has been approved by the local IRB on January 29th 2019 (BASEC 2018-
24 01180) and registered on <http://www.clinicaltrials.gov> with the identifier: NCT03755349. All
25 patients and/or next-of-kin will give written informed consent.

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3 **1 Tables**

4 **Table 1:** Tabular listing of schedule of events and assessments and procedures of the study.
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6 ADLs = activities of daily living; ANA = Aesthetic Numeric Analogue scale; CDG =
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8 Clavien-Dindo grading scale; CT = computed tomography; EQ-5D = EuroQol 5 D health
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10 questionnaire; mRS = modified Rankin Scale; NIHSS = National Institute of Health Stroke
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12 Scale.

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Study Periods	Before surgery	Surgery	Discharge from hospital	90-day Follow-up	12-month Follow-up
Visit	1	2	3	4	5
Time (days)	0 (-7 – 0)	0	5 (3 – 14)	90 (±10)	365 (±30)
Patient Information and Informed Consent	x		(x)	(x)	
Demographics	x				
Medical History	x				
In- /Exclusion Criteria	x				
Physical Examination	x		x	x	
Laboratory Examinations					
Quick/INR/PTT		x			
Thrombocyte count		x			
Randomization	x				
Other examinations (CT-Scan)	x		x	x	
Hematoma volume	x		x	x	
Administer Medical Device (burr hole covers and screws)		x			
Primary outcome					
Patient satisfaction (ANA)				x	x
Secondary outcomes					
Impairment in ADLs				x	x
Skin depression				x	x
HrQoL (EQ-5D)	x			x	x
Disability (mRS)	x		x	x	
Neurological status (NIHSS)	x		x	x	
Complications (CDG)			x	x	x
Adverse Events	x	x	x	x ^B	x

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3 **Figure legends**
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5 **Figure 1:** Example of skin depression above the burr holes in a male patient in his late 80's,
6 about two years following frontal and parietal burr hole trepanation for the evacuation of a
7 large chronic subdural hematoma. The photo was taken with his permission and at this time
8 he continued to lead an active life. Upon inquiry, he and his wife confirmed feeling troubled
9 by the well-visible and stigmatizing skin depressions.
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15 **Figure 2:** Illustration of the algorithm of the CORRECT-SCAR trial. cSDH = chronic
16 subdural hematoma; CT = computed tomography.
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1 **Supplementary digital content**

2 **Supplementary digital content 1:** Standard protocol for cSDH evacuation.

3 **Supplementary digital content 2:** SOP for the application of burr hole covers in the context
4 of cSDH evacuation.

5

For peer review only

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3 **1 Authors' contributions:**

4
5 2 Those persons listed as authors on the manuscript have made substantial contributions to the
6
7 3 conception or design of the work, are currently involved in acquiring, analyzing, or
8
9 4 interpreting the data for the work. They all have been active in drafting or revising the study
10
11 5 protocol for important intellectual content, which is basis of the current article. All authors
12
13 6 have approved the final version to be published. They agree to be accountable for all aspects
14
15 7 of the work in ensuring that questions related to the accuracy or integrity of any part of the
16
17 8 work are appropriately investigated and resolved.

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19 9 In detail: MNS, KA, FV, JV, EJ, PS, SV, OB, NRS, OLB, LR and MRG designed the study,
20
21 10 are local (principle) investigators or other key persons. MNS acquired the funding. MNS
22
23 11 reviewed the literature and drafted the manuscript. KA, FV, JV, EJ, PS, SV, OB, NRS, OLB,
24
25 12 LR and MRG contributed to drafting of the manuscript. All authors read and approved the
26
27 13 final manuscript.

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29 14
30 15 **Funding Statement:**

31
32 16 This research is financed and conducted by the Department of Neurosurgery, University
33
34 17 Hospital Zurich, Switzerland. It is financially supported by the Stryker company, after careful
35
36 18 and independent review of the study protocol. The funding source is not involved and does
37
38 19 not influence the data collection, measurements, interpretation, or drafting of the manuscript.

39
40 20
41 21 **Competing interests statement:**

42
43 22 All authors declare that they have nothing to disclose and no conflicts of interest.

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45 23
46 24 **Data availability statement:**

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48 25 Individual patient data (IPD), study protocol, statistical analysis plan (SAP) and analytic code
49
50 26 will be made available on reasonable request, once the results are published and if approved
51
52 27 by the institutional review board (KEK-ZH).

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54 28
55 29 **Word count:**

56
57 30 3079 for article text (excluding references)

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Example of skin depression above the burr holes in a male patient in his late 80's, about two years following frontal and parietal burr hole trepanation for the evacuation of a large chronic subdural hematoma. The photo was taken with his permission and at this time he continued to lead an active life. Upon inquiry, he and his wife confirmed feeling troubled by the well-visible and stigmatizing skin depressions.

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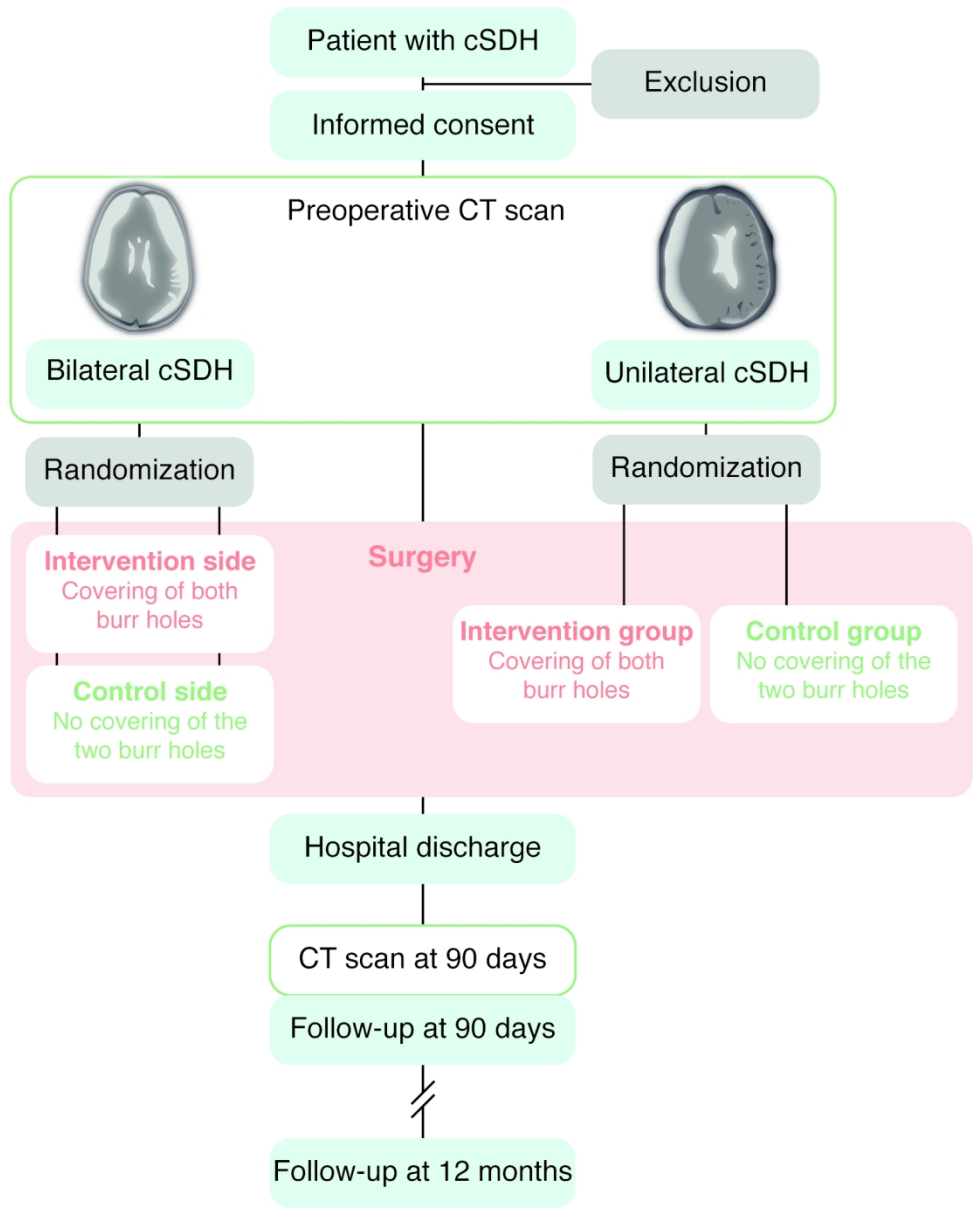


Illustration of the algorithm of the CORRECT-SCAR trial. cSDH = chronic subdural hematoma; CT = computed tomography.



STANDARD OPERATING PROCEDURE

Application of burr-hole covers after trepanation of chronic subdural hematoma

Surgical Procedure in general

The procedure is described for one-sided burr-hole trepanation – but can likewise be applied for bilateral trepanations – of chronic subdural hematomas (cSDH).

1. The procedure is usually performed under general anesthesia.
2. The head is rotated about 80° towards the contralateral side and positioned on a ring-shaped gel cushion.
3. The hair is shaved for 5x2 cm in the region of anticipated incisions.
4. No infiltration of the skin (with saline or local anesthesia).
5. Skin incisions, each one frontal and parietal, about 35 mm in length.
6. Double burr-hole trepanation with the 14-mm trepan.
7. The frontal burr-hole is usually placed at the junction of the superior temporal line and the coronal suture (stephanion), while the posterior burr-hole is usually placed in the region of the parietal eminence.
8. After trepanation and dural opening, the hematoma is evacuated by repeated irrigation with warmed saline solution until reflux is limpid.
9. Per operated side, a subperiosteal drain is placed.
10. The burr-hole cover is now placed and secured with 2 screws, according to the protocol below.
11. The subdural space is filled with warmed saline solution in order to prevent from trapped air inside the skull.
12. The skin is closed by tight subcutaneous sutures and staples on the skin (one staple for each 3 mm incision length).
13. For bilateral cSDH, the procedure is repeated on the contralateral side

Application of the burr-hole cover

The following steps must be taken to prevent from patient injury during application of the burr-hole cover and its fixation with screws. Of note, we usually place the subperiosteal drain before placement of the burr-hole covers, but for demonstration purpose the following pictures were made without the drain (it can gently be pushed aside for the burr-hole cover placement).

1. For each burr-hole that is to be covered, one burr-hole cover (UN3 BURR HOLE COVER, 20mm, W/TAB, Item code 53-34520, Stryker®, Kalamazoo, Michigan; Figures 1 & 2) is applied.



Figure 1: UN3 BURR HOLE COVER, 20mm (Stryker®, Kalamazoo, Michigan) with magnified UNIII AXS SCREWS, SELF-DRILLING, 1.5 x 4MM (Stryker®, Kalamazoo, Michigan).

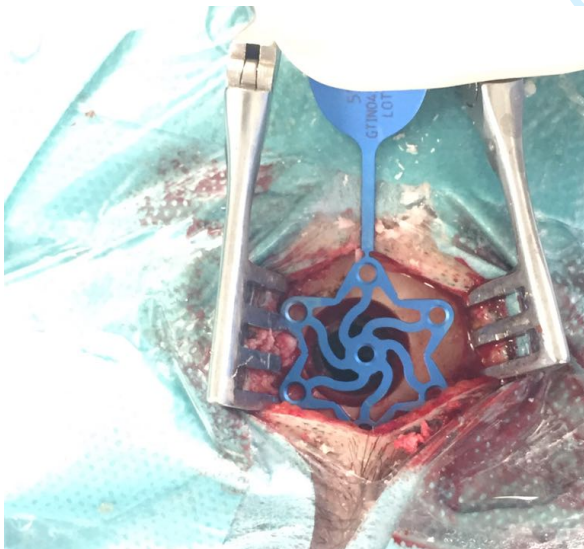


Figure 2: Image demonstrating the placement of UN3 BURR HOLE COVER, 20mm (Stryker®, Kalamazoo, Michigan) in situ.

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2. The burr-hole cover is firmly pressed to the patient skull with the finger, making sure that the burr-hole is completely covered and no items such as screws can fall into the subdural space (Figure 3).



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Figure 3: Image demonstrating how the burr-hole cover is positioned over the burr-hole, using a finger to hold the position.

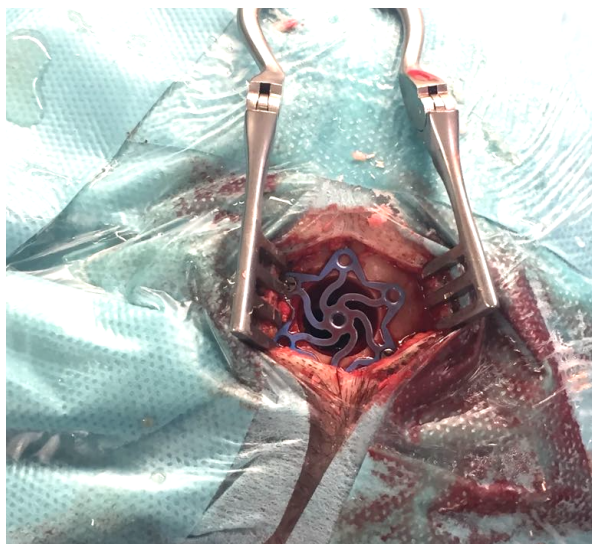
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3. Only when the burr-hole is completely covered, the surgeon receives the first screw (UNIII AXS SCREWS, SELF-DRILLING, 1.5 x 4MM, Item code 56-15934, Stryker®, Kalamazoo, Michigan) and applies it in any given screw hole of the burr-hole cover (Figure 4).



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Figure 4: Image demonstrating how the screw should be applied, with the surgeon making sure that the burr-hole cover covers the burr-hole completely.

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5 4. Only after double-checking that the burr-hole is still completely covered and while
6 continuing to press it onto the patient skull, the surgeon receives the second screw
7 (UNIII AXS SCREWS, SELF-DRILLING, 1.5 x 4MM, Item code 56-15934,
8 Stryker®, Kalamazoo, Michigan) and applies it in the screw hole on the most opposite
9 side (Figure 5).
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32
33 **Figure 5:** Image demonstrating the application of the second screw in the most
34 opposite screw hole of the burr-hole cover.
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39 Authors:

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42 Department of Neurosurgery, University Hospital Zurich, Switzerland
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Standard protocol for chronic subdural hematoma (cSDH) evacuation

All symptomatic patients, particularly those with large cSDH (maximal axial diameter > 15mm or relevant midline shift (MLS)) or presenting in reduced vigilance (GCS < 15) are usually operated within 24 hours. Coagulation parameters are checked routinely prior to surgery. Surgery for patients under anti-aggregation or anticoagulation is delayed until blood clotting and thrombus functions is restored, whenever possible, under close monitoring. Our departmental protocol aims at maintaining platelets at $>100 \times 10^9/\text{dl}$ and an international normalized ratio (INR) of <1.4 . Coagulation abnormalities are actively reversed preoperatively with prothrombin complex concentrate or fresh frozen plasma, if urgent surgery is required. Antiplatelet medication is stopped 5–7 days prior to surgery; if urgent surgery is required, one jumbo unit of platelet concentrate is administered immediately preoperative.

We usually perform double burr-hole trepanation (20mm) per side under general anesthesia. The patient is placed in supine position with the head rotated about 80° towards the contralateral side and positioned on a ring-shaped gel cushion. If necessary, the hair is shaved for 5×2 cm in the region of anticipated incisions. Two skin incisions per side, each 35 mm in length, are required. A 14-mm trepan is used for both burr holes. The frontal burr hole is usually placed at the junction of the superior temporal line and the coronal suture (stephanion), while the posterior burr hole is usually placed in the region of the parietal eminence. In case of significant bilateral hematoma, trepanation is performed on both sides. After trepanation and dural opening, the hematoma is evacuated by repeated irrigation with warmed saline solution until reflux is limpid. There is little doubt that placing a drain after hematoma evacuation can significantly reduce the recurrence rate in cSDH. Whether placing the drain in the superiostal or subdural space is superior has not been proven so far, but we prefer subperiosteal drains for the better safety profile. The skin is closed by tight subcutaneous sutures and staples on the surface. For bilateral cSDH the procedure is repeated on the contralateral side.

Postoperatively, patients remain immobilized and flat in supine position for 48 hours until the drain is removed. In absence of residual deficits, patients are discharged from postoperative day three on. We routinely perform outpatient follow-up visits with cranial computed

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tomography (CT) scan at 6 and 12 weeks postoperatively. Follow-up is continued on an individual basis afterwards.

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SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym - YES
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry - YES
	2b	All items from the World Health Organization Trial Registration Data Set - YES
Protocol version	3	Date and version identifier - YES
Funding	4	Sources and types of financial, material, and other support - YES
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors - YES
	5b	Name and contact information for the trial sponsor - YES
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities - YES
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) - YES
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention - YES
	6b	Explanation for choice of comparators - YES
Objectives	7	Specific objectives or hypotheses - YES

1
2 Trial design 8 Description of trial design including type of trial (eg, parallel group,
3 crossover, factorial, single group), allocation ratio, and framework (eg,
4 superiority, equivalence, noninferiority, exploratory) - **YES**
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8 **Methods: Participants, interventions, and outcomes**
9

10 Study setting 9 Description of study settings (eg, community clinic, academic hospital)
11 and list of countries where data will be collected. Reference to where
12 list of study sites can be obtained - **YES**
13

14 Eligibility criteria 10 Inclusion and exclusion criteria for participants. If applicable, eligibility
15 criteria for study centres and individuals who will perform the
16 interventions (eg, surgeons, psychotherapists) - **YES**
17
18

19 Interventions 11a Interventions for each group with sufficient detail to allow replication,
20 including how and when they will be administered - **YES**
21

22 11b Criteria for discontinuing or modifying allocated interventions for a
23 given trial participant (eg, drug dose change in response to harms,
24 participant request, or improving/worsening disease) - **YES**
25

26 11c Strategies to improve adherence to intervention protocols, and any
27 procedures for monitoring adherence (eg, drug tablet return,
28 laboratory tests) - **YES**
29

30 11d Relevant concomitant care and interventions that are permitted or
31 prohibited during the trial – **NOT APPLICABLE**
32
33

34 Outcomes 12 Primary, secondary, and other outcomes, including the specific
35 measurement variable (eg, systolic blood pressure), analysis metric
36 (eg, change from baseline, final value, time to event), method of
37 aggregation (eg, median, proportion), and time point for each
38 outcome. Explanation of the clinical relevance of chosen efficacy and
39 harm outcomes is strongly recommended - **YES**
40
41

42 Participant 13 Time schedule of enrolment, interventions (including any run-ins and
43 timeline washouts), assessments, and visits for participants. A schematic
44 diagram is highly recommended (see Figure) – **YES – FIGURE 2 &**
45 **TABLE 1**
46
47

48 Sample size 14 Estimated number of participants needed to achieve study objectives
49 and how it was determined, including clinical and statistical
50 assumptions supporting any sample size calculations - **YES**
51

52 Recruitment 15 Strategies for achieving adequate participant enrolment to reach
53 target sample size - **YES**
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56 **Methods: Assignment of interventions (for controlled trials)**
57

58 Allocation:
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1			
2	Sequence	16a	Method of generating the allocation sequence (eg, computer-
3	generation		generated random numbers), and list of any factors for stratification.
4			To reduce predictability of a random sequence, details of any planned
5			restriction (eg, blocking) should be provided in a separate document
6			that is unavailable to those who enrol participants or assign
7			interventions - YES
8			
9			
10	Allocation	16b	Mechanism of implementing the allocation sequence (eg, central
11	concealment		telephone; sequentially numbered, opaque, sealed envelopes),
12	mechanism		describing any steps to conceal the sequence until interventions are
13			assigned - YES
14			
15	Implementation	16c	Who will generate the allocation sequence, who will enrol participants,
16			and who will assign participants to interventions - YES
17			
18			
19	Blinding	17a	Who will be blinded after assignment to interventions (eg, trial
20	(masking)		participants, care providers, outcome assessors, data analysts), and
21			how - YES
22			
23		17b	If blinded, circumstances under which unblinding is permissible, and
24			procedure for revealing a participant's allocated intervention during
25			the trial - YES
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27			

Methods: Data collection, management, and analysis

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30	Data collection	18a	Plans for assessment and collection of outcome, baseline, and other
31	methods		trial data, including any related processes to promote data quality (eg,
32			duplicate measurements, training of assessors) and a description of
33			study instruments (eg, questionnaires, laboratory tests) along with
34			their reliability and validity, if known. Reference to where data
35			collection forms can be found, if not in the protocol - YES
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38		18b	Plans to promote participant retention and complete follow-up,
39			including list of any outcome data to be collected for participants who
40			discontinue or deviate from intervention protocols - YES
41			
42	Data	19	Plans for data entry, coding, security, and storage, including any
43	management		related processes to promote data quality (eg, double data entry;
44			range checks for data values). Reference to where details of data
45			management procedures can be found, if not in the protocol - YES
46			
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48	Statistical	20a	Statistical methods for analysing primary and secondary outcomes.
49	methods		Reference to where other details of the statistical analysis plan can be
50			found, if not in the protocol - YES
51			
52		20b	Methods for any additional analyses (eg, subgroup and adjusted
53			analyses) - YES
54			
55		20c	Definition of analysis population relating to protocol non-adherence
56			(eg, as randomised analysis), and any statistical methods to handle
57			missing data (eg, multiple imputation) - YES
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Methods: Monitoring

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4 Data monitoring 21a Composition of data monitoring committee (DMC); summary of its role
5 and reporting structure; statement of whether it is independent from
6 the sponsor and competing interests; and reference to where further
7 details about its charter can be found, if not in the protocol.
8 Alternatively, an explanation of why a DMC is not needed - **YES**
9
10 21b Description of any interim analyses and stopping guidelines, including
11 who will have access to these interim results and make the final
12 decision to terminate the trial - **YES**
13
14
15 Harms 22 Plans for collecting, assessing, reporting, and managing solicited and
16 spontaneously reported adverse events and other unintended effects
17 of trial interventions or trial conduct - **YES**
18
19 Auditing 23 Frequency and procedures for auditing trial conduct, if any, and
20 whether the process will be independent from investigators and the
21 sponsor - **YES**
22
23

Ethics and dissemination

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25
26 Research ethics 24 Plans for seeking research ethics committee/institutional review board
27 approval (REC/IRB) approval - **YES**
28
29 Protocol 25 Plans for communicating important protocol modifications (eg,
30 amendments changes to eligibility criteria, outcomes, analyses) to relevant parties
31 (eg, investigators, REC/IRBs, trial participants, trial registries, journals,
32 regulators) - **YES**
33
34
35 Consent or assent 26a Who will obtain informed consent or assent from potential trial
36 participants or authorised surrogates, and how (see Item 32) - **YES**
37
38 26b Additional consent provisions for collection and use of participant data
39 and biological specimens in ancillary studies, if applicable – **NOT**
40 **APPLICABLE**
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42
43 Confidentiality 27 How personal information about potential and enrolled participants will
44 be collected, shared, and maintained in order to protect confidentiality
45 before, during, and after the trial - **YES**
46
47 Declaration of 28 Financial and other competing interests for principal investigators for
48 interests the overall trial and each study site - **YES**
49
50 Access to data 29 Statement of who will have access to the final trial dataset, and
51 disclosure of contractual agreements that limit such access for
52 investigators – **NOT APPLICABLE – DATA ACCESS REGULATED**
53 **BY ELECTRONIC GCP-CONFORM DATABASE**
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56 Ancillary and 30 Provisions, if any, for ancillary and post-trial care, and for
57 post-trial care compensation to those who suffer harm from trial participation – **NOT**
58 **APPLICABLE**
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- Dissemination policy
- 31a Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions - **YES**
- 31b Authorship eligibility guidelines and any intended use of professional writers - **YES**
- 31c Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code – **THIS PROTOCOL IS PUBLISHED OPEN ACCESS IN BMJ Open, IF ACCEPTED**

Appendices

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- Informed consent materials
- 32 Model consent form and other related documentation given to participants and authorised surrogates – **NOT HELPFUL TO MOST READERS, AS IN GERMAN LANGUAGE**
- Biological specimens
- 33 Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable - **NOT APPLICABLE**

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COVeRs to impRove EsthetiC ouTcome after Surgery for Chronic subdural hemAtoma by buRr hole trepanation (CORRECT-SCAR) – protocol of a Swiss single-blinded, randomized controlled trial

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Manuscripts

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3 1 **COVeRs to impRove EsthetiC ouTcome after Surgery for Chronic subdural hemAtoma**
4 **by buRr hole trepanation (CORRECT-SCAR) – protocol of a Swiss single-blinded,**
5 **2 randomized controlled trial**
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Abstract

Introduction: Outcomes rated on impairment scales are satisfactory after burr hole trepanation for chronic subdural hematoma (cSDH). However, the surgery leads to bony defects in the skull with skin depressions above that are frequently considered esthetically unsatisfactory by patients. Those defects could be covered by approved medical devices (burr hole covers), but this is rarely done today. We wish to assess, whether the application of burr hole covers after trepanation for the evacuation of cSDH leads to higher patient satisfaction with the esthetical result at 90 days postoperative, without worsening disability outcomes or increasing the complication rate.

Methods and analysis: This is a prospective, single-blinded, randomized, controlled, investigator initiated clinical trial enrolling eighty adult patients with first-time uni- or bilateral cSDH in Switzerland. The primary outcome is the difference in satisfaction with the esthetic result of the scar, comparing patients allocated to the intervention (burr hole cover) and control (no burr hole cover) group, measured on the Aesthetic Numeric Analogue scale at 90 days postoperative. Secondary outcomes include differences in the rates of skin depression, complications, as well as neurological, disability and health-related quality of life outcomes until 12 months postoperative.

Ethics and dissemination: The institutional review board (Kantonale Ethikkommission Zürich) approved this study on January 29th 2019 under case number BASEC 2018-01180. This study determines, whether a relatively minor modification of a standard surgical procedure can improve patient satisfaction, without worsening functional outcomes or increasing the complication rate. The outcome corresponds to the value-based medicine approach of modern patient-centered medicine. Results will be published in peer-reviewed journals and electronic patient data will be safely stored for 15 years.

Trial registration: ClinicalTrials.gov identifier: NCT03755349.

Key words

Burr hole cover; Chronic subdural hematoma; Trepanation; Esthetic outcome; Complications; Scar; Patient satisfaction; Burr hole plate

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3 **Article summary – strengths and limitations of this study**
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- 5 2 - The study might prove that surgeons can positively influence the satisfaction of their
6 3 patients by a minor and inexpensive technical nuance (adding a burr hole cover before
7 4 skin closure).
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9 5 - By randomizing patients with unilateral cSDH into an intervention and control group,
10 6 the effect of potential confounders should be minimized.
11
12 7 - The inclusion of patients with bilateral cSDH allows studying a completely unbiased
13 8 effect of burr hole covers on the outcome of interest (as each patient serves as his/her
14 9 own internal control).
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16 10 - The 90-day period of the primary endpoint may be too short to detect a difference in
17 11 outcome (as skin depressions progressively occur over time), but additional 12-month
18 12 outcome assessment should capture this.
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1 **General Information**

2 Protocol title: COVeRs to impRove EsthetiC ouTcome after Surgery for Chronic subdural
3 hemAtoma by buRr hole trepanation (CORRECT-SCAR) - a single-blinded, randomized
4 controlled trial

5
6 Protocol identifying number: BASEC 2018-01180

7
8 Date of acceptance by institutional review board: January 29th 2019

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1 Introduction

2 Outcome in terms of recovery of impaired neurological function is generally satisfactory after
3 burr hole trepanation for the evacuation of chronic subdural hematoma (cSDH).^{1 2} Despite being
4 considered a relative minimally invasive type of surgery, it requires drilling holes in the
5 patient's skull. With progressive hematoma reabsorption during follow-up, patients may
6 develop skin depressions above the burr hole sites (Figure 1).^{3 4} Theoretically, burr holes could
7 be covered by approved medical devices (burr hole covers) after cSDH evacuation and prior to
8 closing the wound.

9 This has not become standard of care, however, and we previously set out to explore the
10 prevalence and relevance of skin depressions, as well as today's pattern of care by conducting
11 a cross-sectional survey-based study among neurosurgeons globally. Analyzing 576 responses
12 from 78 different countries, 76% of neurosurgeons stated that their patients complained about
13 skin depressions after burr hole trepanations more or less frequently.⁵ In contrary, only 28% of
14 neurosurgeons currently apply burr hole covers more or less frequently for this indication. Their
15 reluctance was mostly explained by a lack of evidence for any proven benefit, less so for the
16 fear of an increased complication rate, technical difficulties and financial reasons. Around three
17 quarters (78% of neurosurgeons) indicated that they would consider applying burr hole covers
18 for this indication, in case a high-quality trial demonstrated its efficacy and safety.⁵

19 We retrospectively reviewed a series of n=28 cSDH patients (64 burr holes) treated at
20 our department, of which n=11 patients had received a burr hole cover on 14 burr holes at the
21 surgeon's discretion. Applying the Aesthetic Numeric Analogue (ANA) scale to rate the
22 esthetical result of the surgery,⁶ patients rated sites where the burr hole was covered more
23 favorably than sites where the burr hole was left uncovered (ANA 9.3±0.74 vs. 7.9±1.0;
24 p<0.001).⁴ In addition, the rates of skin depression were as low as 7% in the intervention group
25 and as high as 92% in the control group (p<0.001). Evidently, the prior results were subject to
26 selection bias, patients were not blinded for the intervention and the study was underpowered
27 to estimate possible group differences in complications.⁴ These preliminary findings were a
28 promising starting point for further and more in-depth research, because filling this knowledge
29 gap is likely to affect future management of cSDH patients.

31 Methods and analysis

32 *Study Goals and Objectives*

33 The CORRECT SCAR trial aims to demonstrate that the placement of burr hole covers on the
34 burr hole sites improves patient satisfaction with the esthetic outcome of the surgical procedure

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3 1 at 3 and 12 months postoperative. It also aims to demonstrate that clinical outcomes (disability,
4 2 neurological function & health-related quality of life (hrQoL)) remain similar and complication
5 3 rates (e.g., surgical site infections (SSIs), cSDH recurrences, etc.) are not increased by applying
6 4 burr hole covers.
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10 5 The primary objective is to compare mean ANA scores (patient satisfaction with the
11 6 esthetic result of the surgery) between the intervention and control group at 90 days
12 7 postoperatively. Secondary/safety objectives are to compare mean ANA scores, rates of skin
13 8 depression, impairment in activities of daily living (ADLs), disability (modified Rankin scale
14 9 (mRS)), hrQoL (Euro-QoL (EQ)-5D), neurological status (National Institute of Health Stroke
15 10 scale (NIHSS)), complications and residual hematoma volume between the intervention and
16 11 control group at 3 and 12 months postoperative.
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24 13 *Study Design*

25 14 Prospective, single-blinded, randomized, controlled, investigator initiated clinical trial. The
26 15 trial is conducted at the University Hospital Zurich, Switzerland. The study will be reported
27 16 according to the CONSORT guidelines.⁷
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31 17 *Eligibility criteria*

32 18 Participants fulfilling all of the following inclusion criteria are eligible for the study:

- 33 19 - Patients with first-time cSDH (hypodense, isodense, hyperdense or mixed-type in CT-
34 20 imaging), scheduled for uni- or bilateral double burr hole trepanation under general
35 21 anesthesia
- 36 22 - Patient age \geq 18 years
- 37 23 - Patient non-comatose at time of inclusion (GCS > 8 points)
- 38 24 - Patient able to communicate (in terms of ability to hear, see, speak and understand).
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47 26 The presence of any one of the following exclusion criteria will lead to exclusion of the
48 27 participant:

- 49 28 - Patient with recurrent cSDH or previous surgery for cSDH
- 50 29 - Patient with cSDH treated by craniotomy or by single burr hole trepanation
- 51 30 - Patient with cSDH treated in local anesthesia
- 52 31 - Patient unlikely to attend the follow-up (due to reasons of residency, dismal prognosis,
53 32 etc.)
- 54 33 - Pregnancy
- 55 34 - Known allergy against or incompatibility with Titanium
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- 1 - Known or suspected non-compliance
- 2 - Inability to follow the study procedures, e.g. due to psychological disorders, dementia, etc. of the participant.

4 *Intervention & study groups*

5 A study algorithm can be found in figure 2 and table 1 outlines all visits and procedures.

6 1. Patients with unilateral cSDH

7 All patients randomized into the control group will be treated according to our standard protocol for cSDH evacuation (supplementary digital content 1).

8 All patients randomized into the intervention group will be treated according to our standard protocol for cSDH evacuation with one exception: placement of a burr hole cover (UN3 BURR HOLE COVER, 20mm, W/TAB, Item code 53-34520, Stryker®, Kalamazoo, Michigan) that is fixed with 2 screws (UNIII AXS SCREWS, SELF-DRILLING, 1.5 x 4MM, Item code 56-15934, Stryker®, Kalamazoo, Michigan) on both burr holes after evacuation of the hematoma and prior to skin closure.

15 2. Patients with bilateral cSDH

16 Patients with bilateral cSDH serve as their own internal control. They are randomized concerning the intervention or control side, being either the side with larger or smaller hematoma, respectively.

19 All patients are blinded concerning the study group/side allocation. For application of the burr hole cover, surgeons will be instructed to firmly press the burr hole cover on the burr hole before receiving the screws from the scrub nurse in order to prevent from screws accidentally falling into the subdural space. For this purpose, a standard operating procedure (SOP) has been developed (supplementary digital content 2). No dexamethasone is applied to surgical candidates who are enrolled into this trial.

25 *Primary Outcome and Follow-Up*

26 For the primary outcome, patient satisfaction with the esthetic results of the scar is determined using a patient-rated outcome measure (PROM), the ANA scale,⁶ ranging from 0 (dissatisfied) – 10 (very satisfied), at 90 days postoperative. The outcome is assessed by mailed questionnaire and collected by a study coordinator.

30 *Secondary Outcomes*

- 31 - Patient satisfaction with the esthetic result of the scar, determined by the ANA scale, at 32 12 months postoperatively (mailed questionnaire, collected by a study coordinator).

- 1 - Impairment in ADLs (e.g., when hairdressing, combing, washing, etc.), rated as “yes”
- 2 vs. “no”, at 90 days and 12 months postoperative (mailed questionnaire, collected by a
- 3 study coordinator).
- 4 - Rate of skin depression, rated as “yes” vs. “no”, at 90 days and 12 months postoperative
- 5 (mailed questionnaire, collected by a study coordinator).
- 6 - Disability, determined by the mRS (ranging from 0 (no disability) to 6 (dead)) at 90
- 7 days.
- 8 - HrQoL, determined by the EQ-5D (allowing the calculation of both the EQ-5D index
- 9 that ranges from -0.074 (worst hrQoL) – 1.00 (best hrQoL) using European norms and
- 10 the EQ-5D VAS (ranging from 0 (worst hrQoL) – 100 mm (best hrQoL)), at 90 days
- 11 and 12 months postoperative (mailed questionnaire, collected by a study coordinator).
- 12 - Neurological outcome, determined by the NIHSS (ranging from 0 (no neurological
- 13 deficit) – 42 (severe neurological deficit)), at 90 days.
- 14 - Home time, as surrogate marker of disability,⁸ at 90 days and 12 months.

16 *Further safety-outcomes are assessed:*

- 17 - Intra- and postoperative complications up to 90 days and 12 months, in particular cSDH
- 18 recurrence and SSIs.
- 19 - Residual cSDH volume in ccm^3 , absolute (ccm^3) and relative (%) cSDH clearance at 90
- 20 days postoperative (measured by two neuroradiologists independently, otherwise not
- 21 involved in the project, using volumetric analysis).

23 *Patient and Public Involvement*

24 Other than recruiting patients admitted to our hospital, it is not intended to involve patients and

25 the public in the design, conduct and reporting of this research.

27 **Ethics and dissemination**

28 Despite the generally favorable risk profile and outcome of burr hole trepanation for cSDH,

29 skin depressions may occur weeks and months after hematoma reabsorption.^{3 4} These are

30 frequently considered esthetically unsatisfactory by patients and may lead to functional

31 restrictions, e.g. when combing, hairdressing or washing. In own clinical experience, patients

32 reported being stared-at for these skin depressions, evoking feelings of astonishment and

33 aversion from both family members and strangers. With an increasing number of senior citizens

34 in good physical/mental health and leading active social lives, the esthetic aspect of outcome

1 gains new importance. Today's elderly patients do no longer content themselves with a basic
2 surgical procedure, but – as informed customers – expect optimal surgical results topped with
3 an excellent service.⁹

4 In theory, burr hole covers represent an effective, easy-to-apply and relatively
5 inexpensive solution to prevent cosmetically and functionally unfavorable skin depressions.⁴
6 Our survey has clearly demonstrated that – in order to improve the acceptance of this technical
7 nuance – its efficiency needs to be demonstrated first (unpublished data, April 2019). Moreover,
8 as the intervention is unlikely to improve any “hard outcome” such as disability or survival,
9 more data should substantiate its safety.

10 We consider a prospective, randomized, blinded and controlled study design optimal to
11 prove a causal relationship between the study intervention and outcome. A clear strength of this
12 study is that patients with bilateral cSDH can be included and serve as their own internal
13 controls. Any retrospective approach to the study question, or applying the burr hole cover in a
14 prospective fashion and comparing it to a (historical) control group is not possible, as the
15 outcome of interest (ANA scale) has not been established in patients before, as well as for the
16 likelihood of selection bias. The study aim corresponds to the value-based medicine approach
17 of modern patient-centered medicine and results shall be published in peer-reviewed journals.

18 *Trial Status*

19 The study has started enrolling patients on January 29th 2019.

21 *Safety Considerations*

22 Burr hole covers are applied according to a SOP (supplementary digital content 2) and the
23 medical device is approved for the studied application. All device deficiencies, (severe) adverse
24 events ((S)AEs) and (severe) adverse device effects ((S)ADEs) are systematically recorded.
25 The Clinical Trials Center (CTC) of the University of Zurich externally monitors the trial.

26 *Follow-up*

27 Participating patients are followed up to 12 months postoperative.

29 *Unblinding*

30 Maintenance of trial treatment randomization codes will be done by the electronic data
31 capturing system (run by the CTC Zurich), using a built-in tool for randomization. Breaking
32 codes is not allowed. Unblinding (and revealing a participant's allocated intervention) towards

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3 1 the patient is permissible only if the trial is suspended, prematurely terminated due to security
4 2 concerns or completed.
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8 4 *Data Managements and Statistical Analysis*

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10 5 The data is hosted by the CTC, University of Zurich. Electronic case report forms (eCRFs) are
11 6 implemented. All data are stored on a server in a dedicated database. A role concept with
12 7 personal passwords (site investigator, statistician, monitor, administrator etc.) regulates
13 8 permission. Electronic patient data will be stored for 15 years until trial completion.
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18 9 *Handling of missing data*

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20 10 First, the risk of missing data will be minimized by regular data reviews, also with an intention
21 11 to identify at risk patients for lack of follow-up data. Even though the effect of skin depression
22 12 is likely more pronounced at 12 months, compared to 90 days postoperative, we intentionally
23 13 chose to select the 90-day time point as primary outcome in order to minimize drop-out.
24 14 Contingency plans foresee home/rehabilitation visits by study personnel to obtain otherwise
25 15 missing data in patients who cannot show up for the planned 90-day or 12-month follow-up.¹⁰
26 16 Patients who die during the study interval (or cannot be evaluated as aphasic or in too poor
27 17 clinical condition) and in whom for this reason the primary endpoint cannot be obtained will
28 18 be recorded as not assessable for the primary outcome. Sensitivity analyses will be performed
29 19 for this study.
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37 20 If, despite the above-mentioned mechanisms, missing data is present we use the
38 21 following protocol: First, mechanisms of missing data are assessed. If the data are deemed
39 22 missing at random, and there is <10-15% of patients with time point missing data, then case
40 23 deletion will be used (and additional patients will be recruited). Second, if the missing data
41 24 mechanism is not at random, multiple imputation will be performed, a well-accepted method
42 25 for intention to treat analysis in RCT with missing outcome data.^{10 11}
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48 26 *Determination of sample size*

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50 27 Based on an expected mean satisfaction score of 9/10 on the ANA in the intervention and 7/10
51 28 on the ANA in the control group, n=37 patients need to be randomized in each study arm in
52 29 order to find a statistically significant difference in the primary outcome with alpha set at 0.05,
53 30 a power of 80% and an estimated standard deviation of 3.⁴ Based on a total sample size of
54 31 2x37=74, with an estimated dropout rate of 10%, we plan to include n=80 patients in total.
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1 *Methods used to minimize bias*

2 A computerized randomization tool, provided by the electronic data capturing system, is used
3 with the only strata being uni- or bilateral cSDH. The random allocation sequence is generated
4 by the CTC, University of Zurich. Study physicians conduct patient enrollment and
5 randomization after basic patient data has been entered into eCRFs. Due to the randomization
6 process, patients with unilateral cSDH are likely to be well balanced for most important
7 parameters that could potentially influence the primary outcome. In patients with bilateral
8 cSDH, each patient serves as his/her own control, which minimizes the risk of bias (=setting
9 similar to that of a n-of-1 clinical trial but without repetitive crossover).^{12 13}

10 Patients with unilateral cSDH will be randomized in a 1:1 fashion into the intervention
11 or control group, respectively. Patients with bilateral cSDH will be randomized in a 1:1 fashion
12 concerning the intervention side, being either the side with more or lesser hematoma size
13 (Figure 2).

14 Patients will be blinded for allocation to the study group/side, but surgeons will not be.
15 Patients will not be aware of the study group/side, since the operation takes place under general
16 anaesthesia. The fact that patients are blinded for the study group allocation will be mentioned
17 in the discharge letter (in order to inform the family physician), and the neurosurgical team of
18 nurses and physicians will also be informed not to “unblind” the patient.

19 The primary endpoint and most of the secondary endpoints will be determined by mailed
20 questionnaires. This way, the patient will not be influenced by the presence of the physician
21 when judging on satisfaction with the esthetical result of the surgery. In addition, all data is
22 collected by a dedicated study coordinator (E.J.), who is not involved in the patient care
23 (=independent outcome assessment).

24 *Primary analysis*

25 The main analysis will be according to the intention to treat (ITT) protocol. An as-treated
26 analysis will be performed, additionally.

27 Satisfaction on the ANA scale for both the frontal and parietal scar are measured
28 separately, but a mean satisfaction score is built by adding the values and dividing the sum by
29 two. For analysis of the primary outcome the results obtained in the intervention group
30 (unilateral cSDH) and on the intervention side (bilateral cSDH) will be combined and compared
31 to the combined results obtained in the control group and on the control side. As the dependent
32 variable is a quantitative variable on an interval scale, a rank-sum test is appropriate to analyze
33 group differences. Even though no formal minimum clinically important difference (MCID) of
34 the ANA-scale has been determined, we powered the study to detect an in-between group

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3 1 difference in outcome of two points, as – abstracted from the numeric rating scale for pain (also
4 ranging between 0 – 10) – a change of two points is considered to be well above the MCID,¹⁴
5 2 therefore resulting in a clinically meaningful improvement for the patient.
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7 4 Subgroup analyses will be made for patients with bald heads vs. patients with scalp hair,
8 5 male vs. female patients, patients < 60 years vs. ≥ 60 years and for patients with bilateral cSDH.
9 6

10 6 *Secondary analyses*

11 7 As the remaining secondary outcomes are not side-specific but reflect the condition of the
12 8 patient as a whole, the remaining secondary analyses will compare results obtained in patients
13 9 with unilateral cSDH randomized into either the intervention or control group.
14 10

15 11 As the safety outcomes are specific for the incision site and side, for the safety analyses
16 12 the results obtained in the intervention group and on the intervention side will be combined and
17 13 compared to the combined results obtained in the control group and on the controlled side.
18 14

19 15 For the outcomes that are quantitative (hrQoL on the EQ-5D) student's t-tests or rank-
20 16 sum tests will be applied, depending on normally distributed data or not. For the outcomes that
21 17 are categorical (type of impairment with ADLs, disability on the mRS, neurological outcome
22 18 on the NIHSS, complications on the CDG) descriptive analyses and chi-square tests will be
23 19 applied. For the outcomes that are binary (impairment with ADLs, skin depression, etc.) logistic
24 20 regression analysis will be performed, calculating the odds ratio (OR) and 95% confidence
25 21 intervals (CIs).
26 22

27 20 *Interim analyses*

28 21 Once data of 50 patients with completed 90-day follow-up data has been collected, the primary
29 22 endpoint and the safety analyses will be performed.
30 23

31 24 *Quality Assurance*

32 25 The study is conducted in accordance with good clinical practice (GCP) guidelines. All source
33 26 data is accessible for monitoring, audits and inspections. Authorities have the right to perform
34 27 inspections and on-site auditing. External monitoring will be performed by the CTC, University
35 28 of Zurich, as detailed in a monitoring plan including pre-study, site initiation, routine
36 29 monitoring and close-out visits, considering local infrastructure, completeness of documents,
37 30 patient safety, adherence to the study protocol, data quality entered into the eCRFs and the trial
38 31 master file.
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40 33 Progress of patient inclusion and data completeness is continuously (at least once every
41 34 two weeks) checked by a study coordinator (E.J.).
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1 *Expected Outcomes of the Study*

2 The study will shed more light on the question, whether patient satisfaction with the esthetic
3 result of the surgical procedure can be improved by adding burr hole covers on the burr holes
4 after trepanation for cSDH. An improvement in patient satisfaction would likely be conferred
5 through the decreased prevalence of skin depressions, as a strong difference in prevalence of
6 skin depressions was previously found in two retrospective studies.^{3,4} The study will moreover
7 allow to understand better, whether the application of burr hole covers increases the risks of
8 complications, e.g. cSDH recurrence or SSIs. Results of the study are likely to affect future
9 management of cSDH patients.⁵

10 *Duration of the project*

11 Recruitment is expected to be completed by the end of January 2021, with final follow-up
12 collected until January 2022. Publication of the final results is expected around six months after
13 last patient out.

14 *Project management*

15 The principle investigators (M.N.S. & M.R.G.) are responsible for patient inclusion, quality of
16 data collection and adherence to the protocol. They are supported by a team of site investigators,
17 a dedicated study coordinator (E.J.), the monitoring staff and the sponsor (L.R.).

18 *Ethics*

19 The study protocol has been approved by the local IRB (Kantonale Ethikkommission Zürich)
20 on January 29th 2019 (BASEC 2018-01180) and registered on <http://www.clinicaltrials.gov>
21 with the identifier: NCT03755349. All patients and/or next-of-kin will give written informed
22 consent to contributing study physicians. Protocol modifications have to be approved by the
23 local IRB and communicated to trial registries. Authorship for publications will be determined
24 according to the recommendation given by the International Committee of Medical Journal
25 Editors (ICMJE). No use of professional writers is planned.

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3 **1 Tables**

4 **Table 1:** Tabular listing of schedule of events and assessments and procedures of the study.
5
6 ADLs = activities of daily living; ANA = Aesthetic Numeric Analogue scale; CDG = Clavien-
7
8 Dindo grading scale; CT = computed tomography; EQ-5D = EuroQol 5 D health questionnaire;
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10 mRS = modified Rankin Scale; NIHSS = National Institute of Health Stroke Scale.
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Study Periods	Before surgery	Surgery	Discharge from hospital	90-day Follow-up	12-month Follow-up
Visit	1	2	3	4	5
Time (days)	0 (-7 – 0)	0	5 (3 – 14)	90 (±10)	365 (±30)
Patient Information and Informed Consent	x		(x)	(x)	
Demographics	x				
Medical History	x				
In- /Exclusion Criteria	x				
Physical Examination	x		x	x	
Laboratory Examinations					
Quick/INR/PTT		x			
Thrombocyte count		x			
Randomization	x				
Other examinations (CT-Scan)	x		x	x	
Hematoma volume	x		x	x	
Administer Medical Device (burr hole covers and screws)		x			
Primary outcome					
Patient satisfaction (ANA)				x	x
Secondary outcomes					
Impairment in ADLs				x	x
Skin depression				x	x
HrQoL (EQ-5D)	x			x	x
Disability (mRS)	x		x	x	
Neurological status (NIHSS)	x		x	x	
Complications (CDG)			x	x	x
Adverse Events	x	x	x	x ^B	x

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3 **Figure legends**
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5 **Figure 1:** Example of skin depression above the burr holes in a male patient in his late 80's,
6 about two years following frontal and parietal burr hole trepanation for the evacuation of a large
7 chronic subdural hematoma. The photo was taken with his permission and at this time he
8 continued to lead an active life. Upon inquiry, he and his wife confirmed feeling troubled by
9 the well-visible and stigmatizing skin depressions.
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15 **Figure 2:** Illustration of the algorithm of the CORRECT-SCAR trial. cSDH = chronic subdural
16 hematoma; CT = computed tomography.
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1 **Supplementary digital content**

2 **Supplementary digital content 1:** Standard protocol for cSDH evacuation.

3 **Supplementary digital content 2:** SOP for the application of burr hole covers in the context
4 of cSDH evacuation.

5

For peer review only

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3 **1 Authors' contributions:**

4
5 2 Those persons listed as authors on the manuscript have made substantial contributions to the
6
7 3 conception or design of the work, are currently involved in acquiring, analyzing, or interpreting
8
9 4 the data for the work. They all have been active in drafting or revising the study protocol for
10
11 5 important intellectual content, which is basis of the current article. All authors have approved
12
13 6 the final version to be published. They agree to be accountable for all aspects of the work in
14
15 7 ensuring that questions related to the accuracy or integrity of any part of the work are
16
17 8 appropriately investigated and resolved.

18
19 9 In detail: MNS, KA, FV, JV, EJ, PS, SV, OB, NRS, OLB, LR and MRG designed the study,
20
21 10 are local (principle) investigators or other key persons. MNS acquired the funding. MNS
22
23 11 reviewed the literature and drafted the manuscript. KA, FV, JV, EJ, PS, SV, OB, NRS, OLB,
24
25 12 LR and MRG contributed to drafting of the manuscript. All authors read and approved the final
26
27 13 manuscript.

28
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30
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32
33 17 Hospital Zurich, Switzerland. It is financially supported by the Stryker company, after careful
34
35 18 and independent review of the study protocol. The funding source is not involved and does not
36
37 19 influence the data collection, measurements, interpretation, or drafting of the manuscript.

38
39 21 **Competing interests statement:**

40
41 22 All authors declare that they have nothing to disclose and no conflicts of interest.

42
43 24 **Data availability statement:**

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45 25 Individual patient data (IPD), study protocol, statistical analysis plan (SAP) and analytic code
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47 26 will be made available on reasonable request, once the results are published and if approved by
48
49 27 the institutional review board (KEK-ZH).

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51 29 **Word count:**

52
53 30 3364 for article text (excluding references)

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55 31



Example of skin depression above the burr holes in a male patient in his late 80's, about two years following frontal and parietal burr hole trepanation for the evacuation of a large chronic subdural hematoma. The photo was taken with his permission and at this time he continued to lead an active life. Upon inquiry, he and his wife confirmed feeling troubled by the well-visible and stigmatizing skin depressions.

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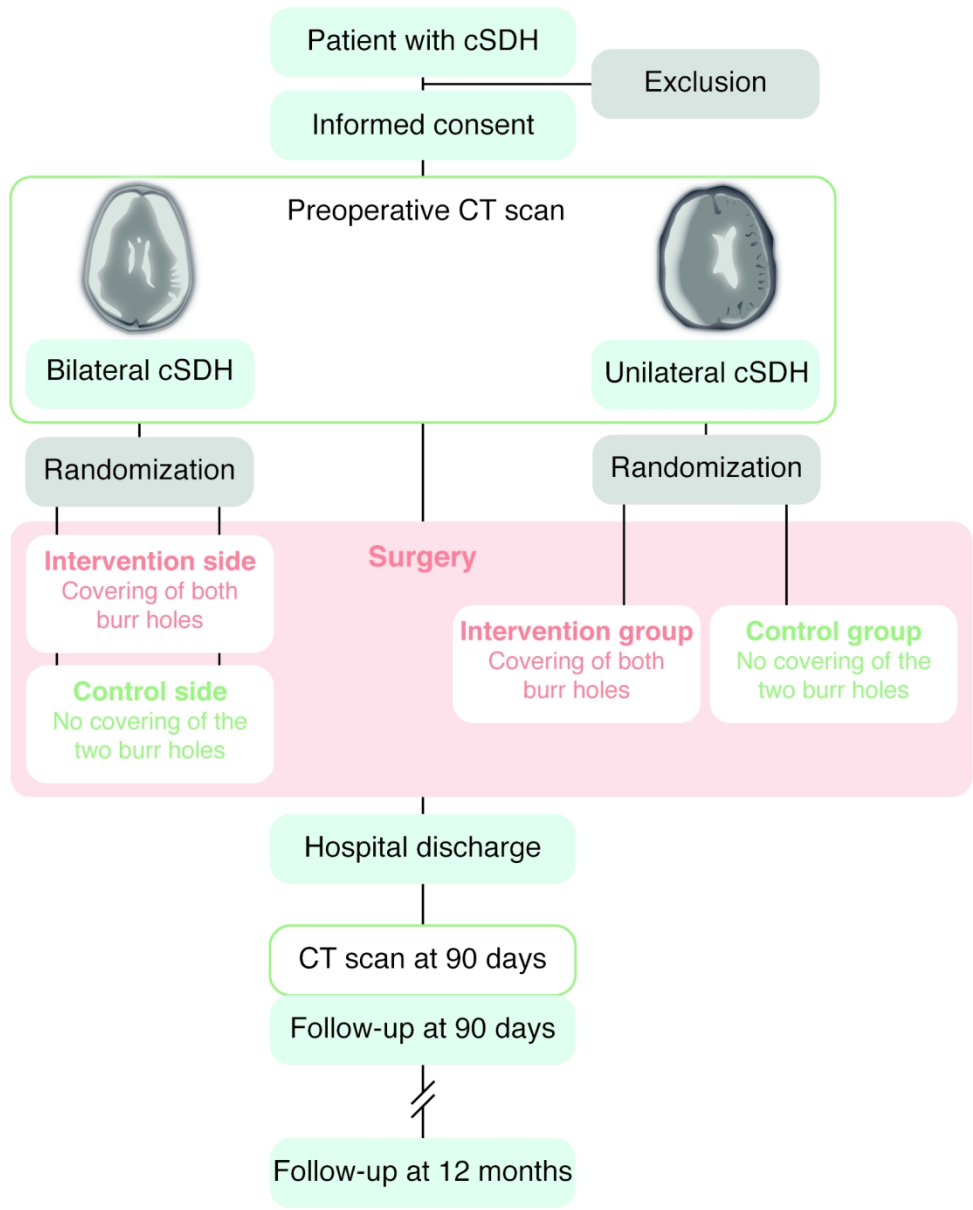


Illustration of the algorithm of the CORRECT-SCAR trial. cSDH = chronic subdural hematoma; CT = computed tomography.



STANDARD OPERATING PROCEDURE

Application of burr-hole covers after trepanation of chronic subdural hematoma

Surgical Procedure in general

The procedure is described for one-sided burr-hole trepanation – but can likewise be applied for bilateral trepanations – of chronic subdural hematomas (cSDH).

1. The procedure is usually performed under general anesthesia.
2. The head is rotated about 80° towards the contralateral side and positioned on a ring-shaped gel cushion.
3. The hair is shaved for 5x2 cm in the region of anticipated incisions.
4. No infiltration of the skin (with saline or local anesthesia).
5. Skin incisions, each one frontal and parietal, about 35 mm in length.
6. Double burr-hole trepanation with the 14-mm trepan.
7. The frontal burr-hole is usually placed at the junction of the superior temporal line and the coronal suture (stephanion), while the posterior burr-hole is usually placed in the region of the parietal eminence.
8. After trepanation and dural opening, the hematoma is evacuated by repeated irrigation with warmed saline solution until reflux is limpid.
9. Per operated side, a subperiosteal drain is placed.
10. The burr-hole cover is now placed and secured with 2 screws, according to the protocol below.
11. The subdural space is filled with warmed saline solution in order to prevent from trapped air inside the skull.
12. The skin is closed by tight subcutaneous sutures and staples on the skin (one staple for each 3 mm incision length).
13. For bilateral cSDH, the procedure is repeated on the contralateral side

Application of the burr-hole cover

The following steps must be taken to prevent from patient injury during application of the burr-hole cover and its fixation with screws. Of note, we usually place the subperiosteal drain before placement of the burr-hole covers, but for demonstration purpose the following pictures were made without the drain (it can gently be pushed aside for the burr-hole cover placement).

1. For each burr-hole that is to be covered, one burr-hole cover (UN3 BURR HOLE COVER, 20mm, W/TAB, Item code 53-34520, Stryker®, Kalamazoo, Michigan; Figures 1 & 2) is applied.



Figure 1: UN3 BURR HOLE COVER, 20mm (Stryker®, Kalamazoo, Michigan) with magnified UNIII AXS SCREWS, SELF-DRILLING, 1.5 x 4MM (Stryker®, Kalamazoo, Michigan).

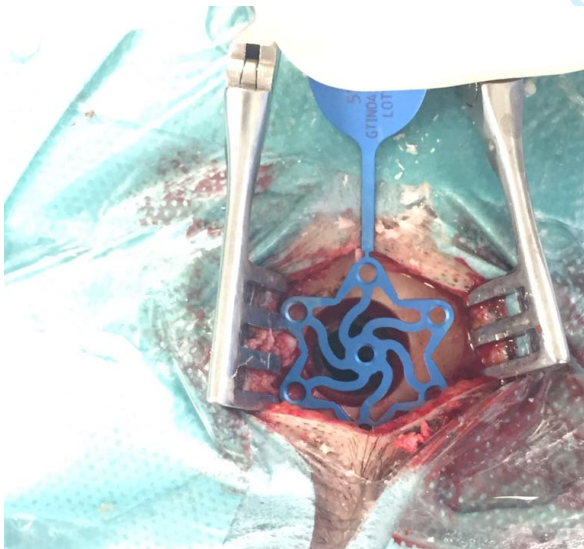


Figure 2: Image demonstrating the placement of UN3 BURR HOLE COVER, 20mm (Stryker®, Kalamazoo, Michigan) in situ.

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 - 2.
- The burr-hole cover is firmly pressed to the patient skull with the finger, making sure that the burr-hole is completely covered and no items such as screws can fall into the subdural space (Figure 3).



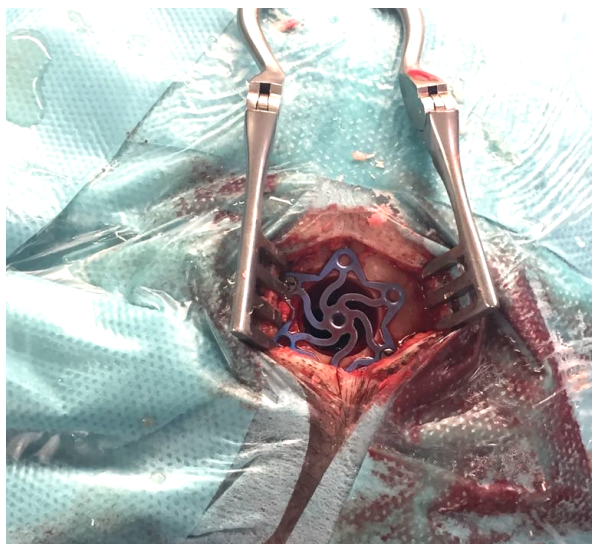
Figure 3: Image demonstrating how the burr-hole cover is positioned over the burr-hole, using a finger to hold the position.

- 3.
- Only when the burr-hole is completely covered, the surgeon receives the first screw (UNIII AXS SCREWS, SELF-DRILLING, 1.5 x 4MM, Item code 56-15934, Stryker®, Kalamazoo, Michigan) and applies it in any given screw hole of the burr-hole cover (Figure 4).



Figure 4: Image demonstrating how the screw should be applied, with the surgeon making sure that the burr-hole cover covers the burr-hole completely.

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5 4. Only after double-checking that the burr-hole is still completely covered and while
6 continuing to press it onto the patient skull, the surgeon receives the second screw
7 (UNIII AXS SCREWS, SELF-DRILLING, 1.5 x 4MM, Item code 56-15934,
8 Stryker®, Kalamazoo, Michigan) and applies it in the screw hole on the most opposite
9 side (Figure 5).
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33 **Figure 5:** Image demonstrating the application of the second screw in the most
34 opposite screw hole of the burr-hole cover.
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39 Authors:

40 Martin N. Stienen, Menno R. Germans, Julia Velz, Flavio Vasella, Luca Regli
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42 Department of Neurosurgery, University Hospital Zurich, Switzerland
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Standard protocol for chronic subdural hematoma (cSDH) evacuation

All symptomatic patients, particularly those with large cSDH (maximal axial diameter > 15mm or relevant midline shift (MLS)) or presenting in reduced vigilance (GCS < 15) are usually operated within 24 hours. Coagulation parameters are checked routinely prior to surgery. Surgery for patients under anti-aggregation or anticoagulation is delayed until blood clotting and thrombus functions is restored, whenever possible, under close monitoring. Our departmental protocol aims at maintaining platelets at $>100 \times 10^9/\text{dl}$ and an international normalized ratio (INR) of <1.4 . Coagulation abnormalities are actively reversed preoperatively with prothrombin complex concentrate or fresh frozen plasma, if urgent surgery is required. Antiplatelet medication is stopped 5–7 days prior to surgery; if urgent surgery is required, one jumbo unit of platelet concentrate is administered immediately preoperative.

We usually perform double burr-hole trepanation (20mm) per side under general anesthesia. The patient is placed in supine position with the head rotated about 80° towards the contralateral side and positioned on a ring-shaped gel cushion. If necessary, the hair is shaved for 5×2 cm in the region of anticipated incisions. Two skin incisions per side, each 35 mm in length, are required. A 14-mm trepan is used for both burr holes. The frontal burr hole is usually placed at the junction of the superior temporal line and the coronal suture (stephanion), while the posterior burr hole is usually placed in the region of the parietal eminence. In case of significant bilateral hematoma, trepanation is performed on both sides. After trepanation and dural opening, the hematoma is evacuated by repeated irrigation with warmed saline solution until reflux is limpid. There is little doubt that placing a drain after hematoma evacuation can significantly reduce the recurrence rate in cSDH. Whether placing the drain in the superiostal or subdural space is superior has not been proven so far, but we prefer subperiosteal drains for the better safety profile. The skin is closed by tight subcutaneous sutures and staples on the surface. For bilateral cSDH the procedure is repeated on the contralateral side.

Postoperatively, patients remain immobilized and flat in supine position for 48 hours until the drain is removed. In absence of residual deficits, patients are discharged from postoperative day three on. We routinely perform outpatient follow-up visits with cranial computed

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tomography (CT) scan at 6 and 12 weeks postoperatively. Follow-up is continued on an individual basis afterwards.

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STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym – YES, page 1 II 1-3
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry – YES, page 3 line 24
	2b	All items from the World Health Organization Trial Registration Data Set – YES, all 20 points are mentioned on various pages of the manuscript
Protocol version	3	Date and version identifier – YES, page 5 line 6
Funding	4	Sources and types of financial, material, and other support – YES, page 5 II 26-27 & page 19 II 15-19
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors – YES, page 5 II 10-31
	5b	Name and contact information for the trial sponsor – YES, page 5 II 10-12
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities – YES, page 19 II 2-13
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) – YES, page 14 II 18-21
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention – YES, page 6 II 1-30

1		6b	Explanation for choice of comparators – YES, page 10 II 10-17
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4	Objectives	7	Specific objectives or hypotheses – YES, page 7 II 1-6
5			
6	Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) – YES, page 7 II 16-18
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12	Methods: Participants, interventions, and outcomes		
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14	Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained – YES, page 7 II 15 - 18
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18	Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) – YES, page 7 I 19 – page 8 I 5
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24	Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered – YES, page 8 II 6 - 25
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29		11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) – YES, page 10 II 30ff
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34		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) – YES, page 11 II 9ff
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39		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial – NOT APPLICABLE
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42	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended – YES, page 8 line 26 ff
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50	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) – YES – FIGURE 2 & TABLE 1, page 10 line 19 & page 14 II 14ff
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56	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations – YES, page 11 II 26ff
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2 Recruitment 15 Strategies for achieving adequate participant enrolment to reach
3 target sample size – **YES, part of the quality assurance – page 13 II**
4 **27ff**
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6 **Methods: Assignment of interventions (for controlled trials)**
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8 Allocation:
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10 Sequence 16a Method of generating the allocation sequence (eg, computer-
11 generation generated random numbers), and list of any factors for stratification.
12 To reduce predictability of a random sequence, details of any planned
13 restriction (eg, blocking) should be provided in a separate document
14 that is unavailable to those who enrol participants or assign
15 interventions – **YES, page 12 II 2 ff**
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18 Allocation 16b Mechanism of implementing the allocation sequence (eg, central
19 concealment telephone; sequentially numbered, opaque, sealed envelopes),
20 mechanism describing any steps to conceal the sequence until interventions are
21 assigned – **YES, page 12 II 2 ff**
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24 Implementation 16c Who will generate the allocation sequence, who will enrol participants,
25 and who will assign participants to interventions – **YES, page 12 II 2 ff**
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27 Blinding 17a Who will be blinded after assignment to interventions (eg, trial
28 (masking) participants, care providers, outcome assessors, data analysts), and
29 how – **YES, page 12 II 2 ff**
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31 17b If blinded, circumstances under which unblinding is permissible, and
32 procedure for revealing a participant's allocated intervention during
33 the trial – **YES, page 10 II 30ff**
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36 **Methods: Data collection, management, and analysis**
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38 Data collection 18a Plans for assessment and collection of outcome, baseline, and other
39 methods trial data, including any related processes to promote data quality (eg,
40 duplicate measurements, training of assessors) and a description of
41 study instruments (eg, questionnaires, laboratory tests) along with
42 their reliability and validity, if known. Reference to where data
43 collection forms can be found, if not in the protocol – **YES, page 15**
44 **table 1**
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47 18b Plans to promote participant retention and complete follow-up,
48 including list of any outcome data to be collected for participants who
49 discontinue or deviate from intervention protocols – **YES, part of**
50 **quality assurance on page 13 II 27ff**
51

52 Data 19 Plans for data entry, coding, security, and storage, including any
53 management related processes to promote data quality (eg, double data entry;
54 range checks for data values). Reference to where details of data
55 management procedures can be found, if not in the protocol – **YES,**
56 **page 11 II 4-8**
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- Statistical methods 20a Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol – **YES, page 12 line 24 – page 13, line 4**
- 20b Methods for any additional analyses (eg, subgroup and adjusted analyses) – **YES, page 12 II 5-22**
- 20c Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) – **YES, page 11 II 9-25**

14 **Methods: Monitoring**

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- Data monitoring 21a Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed – **YES, page 13 II 27ff**
- 21b Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial – **YES, page 13 II 23-25**
- Harms 22 Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct – **YES, page 13 II 8ff**
- Auditing 23 Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor – **YES, page 13 II 27ff**

38 **Ethics and dissemination**

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- Research ethics approval 24 Plans for seeking research ethics committee/institutional review board (REC/IRB) approval – **YES, page 14 II 22-26**
- Protocol amendments 25 Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) – **YES, page 14 II 22ff**
- Consent or assent 26a Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) - **YES, page 14 II 22ff**
- 26b Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable – **NOT APPLICABLE**

1			
2	Confidentiality	27	How personal information about potential and enrolled participants will
3			be collected, shared, and maintained in order to protect confidentiality
4			before, during, and after the trial – YES, page 11 II 4-8
5			
6	Declaration of	28	Financial and other competing interests for principal investigators for
7	interests		the overall trial and each study site – YES, page 19 II 21-22
8			
9	Access to data	29	Statement of who will have access to the final trial dataset, and
10			disclosure of contractual agreements that limit such access for
11			investigators – NOT APPLICABLE – DATA ACCESS REGULATED
12			BY ELECTRONIC GCP-CONFORM DATABASE contained on page
13			11 II 4-8
14			
15			
16	Ancillary and	30	Provisions, if any, for ancillary and post-trial care, and for
17	post-trial care		compensation to those who suffer harm from trial participation – NOT
18			APPLICABLE
19			
20			
21	Dissemination	31a	Plans for investigators and sponsor to communicate trial results to
22	policy		participants, healthcare professionals, the public, and other relevant
23			groups (eg, via publication, reporting in results databases, or other
24			data sharing arrangements), including any publication restrictions –
25			YES, page 19 II 24ff, page 10 line 17
26			
27			
28		31b	Authorship eligibility guidelines and any intended use of professional
29			writers – YES, page 14, II 27ff
30			
31		31c	Plans, if any, for granting public access to the full protocol, participant-
32			level dataset, and statistical code – THIS PROTOCOL IS
33			PUBLISHED OPEN ACCESS IN BMJ Open, IF ACCEPTED. Further
34			information on page 19 II 24ff
35			
36			
37	Appendices		
38			
39	Informed consent	32	Model consent form and other related documentation given to
40	materials		participants and authorised surrogates – NOT HELPFUL TO MOST
41			READERS, AS IN GERMAN LANGUAGE
42			
43	Biological	33	Plans for collection, laboratory evaluation, and storage of biological
44	specimens		specimens for genetic or molecular analysis in the current trial and for
45			future use in ancillary studies, if applicable - NOT APPLICABLE
46			

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](https://creativecommons.org/licenses/by-nc-nd/3.0/)" license.