analysis assuming that patients continuing statins would have an annual ICH recurrence rate of 22% (i.e. 2500 to 3080 subjects) vs. 14% (i.e. 1600 to 1960 subjects) in those who discontinue statins [15]; discontinuing statins could lead to 900-1120 fewer ICHs each year, i.e. $9,180,000 to $24,192,000 less expenditure towards recurrent ICH-related care in addition to approximately $13,248,000 to $16,128,000 towards statin costs. This study could also lead to the validation of genetic markers as tools to assist with decision-making regarding the use of statins in ICH patients.

3. STUDY DESIGN

OVERVIEW OF STUDY DESIGN:

This is a multi-center, pragmatic, prospective, randomized, open-label, and blinded end-point assessment (PROBE) clinical trial. A total of 1456 patients presenting within 7 days of a spontaneous lobar ICH while taking statins will be randomized to one of two treatment strategies: discontinuation vs. continuation of statin therapy (using the same agent and dose that they were using at ICH onset unless a change in statin agent and/or dosing is required for clinical purposes). No placebo will be prescribed for those randomized to discontinue statins. Randomization will balance the treatment distribution according to the following baseline covariates: clinical site, statin dose and indication (primary vs. secondary prevention), current use or intent-to-use oral anticoagulants (OAC) and/or antiplatelets in the long-term post-ICH, and severity of ICH upon presentation as assessed by baseline ICH volume [57]. Participating subjects will undergo baseline testing for APOE genotype and will be followed for up to 24 months to assess for the occurrence of recurrent symptomatic ICH and MACCE.

Follow-up assessments will be performed at 1, 2, 3, 6, 9, 12, 18, and 24 months. All follow-up assessments will be performed via phone (or postal mail if necessary) by centralized and dedicated evaluators. A structured questionnaire will be used to identify recurrent ICH or MACCE resulting in hospitalization and mortality during the follow-up period [see appendix I]; the telephone Montreal Cognitive Assessment (T-MoCA) [54; see appendix II], modified Rankin Scale (mRS) [see appendix III], and EQ-5d [see appendix IV] will also be administered. Verification of statin prescription refills will be performed [see appendix I]. A central adjudication committee blinded to treatment allocation will adjudicate all outcome events, and will review and adjudicate all imaging data.

In cases where the participant prefers to use a virtual platform, instead of telephone, StarLeaf, or Zoom (both 21 CFR part 11-compliant virtual secure platform) will be used to complete these assessments. None of these assessments will be recorded.

SELECTION AND ENROLLMENT OF SUBJECTS:

Study subjects will be recruited from the inpatient services of approximately 140 hospitals in the United States and Canada, under the responsibility of the site investigators. Patients with diagnosis of spontaneous lobar ICH, as confirmed by CT scan, who were taking a statin at the time of ICH onset will be prospectively enrolled, according to the following eligibility criteria.

INCLUSION CRITERIA:

1. Age ≥ 50 years.
2. Spontaneous lobar ICH within 7 days prior to randomization confirmed by CT or MRI scan. Lobar ICH will be defined as ICH involving cortical or subcortical locations and situated ≥1 cm from the body of the ipsilateral lateral ventricle and not originating from any of the following deep structures (thalamus, putamen, globus pallidus, caudate, or internal capsule). Patients with superficial cerebellar ICH, particularly in whom MRI shows lobar cerebral microbleeds suggestive of CAA, can be eligible.
3. Patient was taking a statin drug at the onset of the qualifying/index ICH

4. Randomization must be carried out within 7 days of the onset of the qualifying ICH
5. Patient or legally authorized representative, after consultation with physicians prescribing statin, agrees to be randomized to statin continuation (restart) vs. discontinuation.

EXCLUSION CRITERIA:

1. Suspected secondary cause for the qualifying ICH, such as an underlying vascular abnormality or tumor, trauma, venous infarction, or hemorrhagic transformation of an ischemic infarct.
2. History of recent myocardial infarction (attributed to coronary artery disease) or unstable angina within the previous 3 months
3. Diabetic patients with history of myocardial infarction or coronary revascularization
4. History of familial hypercholesterolemia
5. Patients receiving proprotein convertase subtilisin kexin 9 (PCSK9) inhibitors
6. Known diagnosis of severe dementia
7. Inability to obtain informed consent
8. Patient known or suspected of not being able to comply with the study protocol due to alcoholism, drug dependency, or other obvious reasons for noncompliance, such as unable to adhere to the protocol specified visits/assessments.
9. Life expectancy of less than 24 months due to co-morbid terminal conditions.
10. Pre-morbid mRS >3
11. ICH score >3 upon presentation.
12. Contraindications to continuation/resumption of statin therapy, such as significant elevations of serum creatinine kinase and/or liver transaminases, and rhabdomyolysis
13. Women of childbearing potential, defined as pre-menopausal women capable of becoming pregnant (Post-menopausal women, women who are surgically sterilized, and women who are known to be infertile can be enrolled in the trial).
14. Concurrent participation in another research protocol for investigation of experimental therapy.
15. Indication that withdrawal of care will be implemented for the qualifying ICH.

Participants in SATURN MRI must meet all of the above eligibility criteria, in addition to:

- Subject or surrogate agrees to participate in the MRI study and provides signed informed consent. The option to participate in SATURN MRI will be included as part of the informed consent form for the SATURN trial.
- Subject has no known contraindications to MRI such as claustrophobia, metal implants, or pacemaker.

STUDY ENROLLMENT PROCEDURES:

SCREENING FOR POTENTIAL SUBJECTS:

Subjects will be recruited from inpatients admitted to the stroke units, neurosurgical services, and intensive care units of participating hospitals. Therefore, members of the stroke team and Neurology/Neurosurgery and Neuro ICU residents and staff should be made aware of this study and in-serviced about its protocol to facilitate recruitment. It is expected that the study team and study coordinator (or other designated members of the study staff) will be informed about all patients who are admitted with ICH confirmed by CT; these patients will be reviewed by appropriate members of the study staff within 24 hours of their admission to determine eligibility for participation in the study.

The investigators at each site will be required to maintain a screen failure log for ICH patients who are found ineligible to participate in the study, documenting the patients' age, demographics, and the reason(s) for exclusion from the current study. The study coordinator at