Reviewer's report

Title: Observational Dutch Young Symptomatic StrokE studY (ODYSSEY): study rationale and protocol of a multicentre prospective cohort study.

Version: 2  
Date: 23 December 2013

Reviewer: Sami Curtze

Reviewer's report:

This publication presents a study rationale and protocol of a multicentre prospective cohort study that has not yet started. The aim of the research is an important question and worth investigating. There are many secondary endpoints that will give very useful information as well. A number of 1500 subjects to be recruited seems realistic and plausible. From the authors’ review response letter I found this sentence: “We have no trial-registration as our study is a multicenter prospective cohort.”

1) I would just like to encourage the study team to register the trial f.e. at clinicaltrials.gov or similar space. A similar study, the SECRETO study “Searching for Explanations for Cryptogenic Stroke in the Young: Revealing the Etiology, Triggers, and Outcome” has been registered there. The SECRETO trial focuses on “cryptogenic” strokes in the young. There would be possibility for co-operation. Advantage of registering the “ODYSSEY” trial would increase awareness of the study and new opportunities to join forces will appear.

If recruitment is as expected this study has the possibility to succeed. Details provided are sufficient to allow replication of the work or comparison with related analyses. The manuscript adheres to the relevant standards for reporting and data. The writing is acceptable. There might be a few flaws, f.e.

2) On page 4 last sentence: “of great important as well”. Shouldn’t it be “of great importance as well”?

Specific comments:

3) Classification of intracerebral haemorrhage: Unfortunately there is no good “etiological classification” comparable to TOAST for ICH at present. I would prefer if “hypertensive” would not be used as an etiologic entity. Hypertension is a risk factor for ischemic and for hemorrhagic stroke but it is not the etiology. Would you mind to call it f.e. microangiopathy? Additionally I think the etiology of “bleeding disorder” a little bit dangerous, as f.e. people with anticoagulation can do well without bleeding even with high INR levels and then suddenly get an large ICH while INR is between 2.0-3.0. Ethiology might then as well be microangiopathy or something else but bleeding disorder just prevents the bleeding from stopping to bleed or makes it just clinically significant while otherwise it would have been “silent” microbleed. I agree that your suggested
classification seems to be fine right now, but hopefully well get a new
classification before your study results are published and therefore it would be
better to be warranted not to use “bleeding disorder” too liberally.

4) Additional files/ risk factors: “Hypertension will be defined as a systolic blood
pressure #140 mmHg or diastolic blood pressure #90 [56, 57] or the use of
antihypertensive drugs. “
Can you specify how many repeated measurements and in which timeframe of
RR > 140/90 are needed for the diagnosis of hypertension.

5) table 1. Can you specify “recreational drugs”? Well you specifically question
i.v. drugs, cocain, amphetamine etc?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
Involved in the SECRETo study that has already started. We have a similar focus
but only cryptogenic strokes in the young. Approx 30-40% of the ODYSSEY
population would be suitable for our study as well.