Date: 20-01-2016

Title assignment:
Developing a decision analytic model to determine the impact of (re)starting novel oral anticoagulants (NOACs) in patients with intracerebral hemorrhage (ICH) and atrial fibrillation

Background research / research problem:
The use of (novel) oral anticoagulants may increase both the likelihood and the mortality of intracerebral hemorrhage (ICH), particularly in patients with a history of prior ICH. However, certain patient groups, for example patients with nonvalvular atrial fibrillation, do have a clear indication for anticoagulation. In these patients it is unclear whether after an ICH the benefits of (re)starting anticoagulation exceed the associated risk of harm. Investigating this question in a randomized trial is likely to be infeasible from an ethical perspective. Therefore, a decision analytic model was developed in 2003 to assess the health benefits of (re)starting anticoagulation in patients with a clear indication, following ICH (Eckman et al. Stroke. 2003;34:1710-1716. http://stroke.ahajournals.org/content/34/7/1710.full.pdf). With this model the expected values of 2 treatment strategies —warfarin and no anticoagulation — were compared, for patients with different locations of the ICH. It was concluded that For patients with prior lobar ICH, withholding anticoagulation therapy was strongly preferred, improving quality-adjusted life expectancy by 1.9 QALYs. For patients with prior deep hemispheric ICH, withholding anticoagulation resulted in a smaller gain of 0.3 QALYs. Consequently it was recommended that Survivors of lobar ICH with atrial fibrillation should not be offered long-term anticoagulation. Similarly, most patients with deep hemispheric ICH and atrial fibrillation should not receive anticoagulant therapy. However, patients with deep hemispheric ICH at particularly high risk for thromboembolic stroke or low risk of ICH recurrence might benefit from long-term anticoagulation.

Given clinical developments, and in particular the availability of novel oral anticoagulants (NOACs), such as for example, dabigatran, the balance between benefits and risks of anticoagulation in these patients has likely changed. NOACs have been shown to be as good or possibly better than the traditional anticoagulants (coumarins such as warfarin) with less serious side effects (see for example the editorial by Werdan et al. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3782018/pdf/Dtsch_Arztebl_Int-110-0523.pdf).

Therefore it is now time to perform a new decision analysis to support anticoagulation decision in in patients with intracerebral hemorrhage (ICH) and atrial fibrillation, which accurately reflects recent evidence and treatment processes. The possibility exists that the researchers involved in the original 2003 decision analysis may also collaborate in this project.
Global research goals
In this project, you will develop a new decision analytic model, using the 2003 model as starting point. This will consist of the following steps:

- Perform a literature review on recent evidence regarding a) the consequences and treatment strategies for patients with ICH, b) the cost, effectiveness, and side effects of NOACs, and c) the quality of life, survival, and risk of recurrent ICH in patients with ICH and atrial fibrillation.
- Create a new decision analytic model by first recreating the 2003 model and then extending it to reflect current clinical practice.
- Use the decision analytic model to determine in which (subgroups) of these patients (re)starting NOACs is expected to be beneficial in terms of health outcomes, and in which (subgroups) of these patients it may be cost-effective.
- Use the decision analytic model to determine if additional data collecting (in future studies) would be worthwhile, and what particular data would be most valuable, using value of information analysis.

Methods to be used in broad outline
During this assignment you will become familiar with the literature on ICH, atrial fibrillation, NOACs, and simulation modeling. You will gain insight into the treatment and follow up processes of patients with ICH. You will need to develop the simulation model, preferably in Excel, to allow easy access and changing of underlying assumptions for other researchers and clinicians.

Expected end result
- Report in the layout of a scientific research article
- Recommendations for the use of NOACs in this patient group
- Recommendations for future research

Connection of the assignment with the following Health Sciences courses:
Health Economics, Clinical Efficacy & Medical Technology Assessment; Medical Decision Making; These courses teach on clinical processes, technology assessment and health economic modeling which are the key aspects of this assignment.

Specific knowledge/expertise that is required:
- Interest in health economic and decision analytic modeling
- Knowledge of the basics of simulation modeling and programming is required, for example in R, Excel (VBA), Plant Simulation, or other modeling software environments.

Supervisors (also external supervisors if applicable):
- Dr. ir. Erik Koffijberg, associate professor, Health Technology & Services Research – (UT)
- Dr. Marieke Wermer, neurologist, LUMC

Period that the assignment is available:
- Until May 2016

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