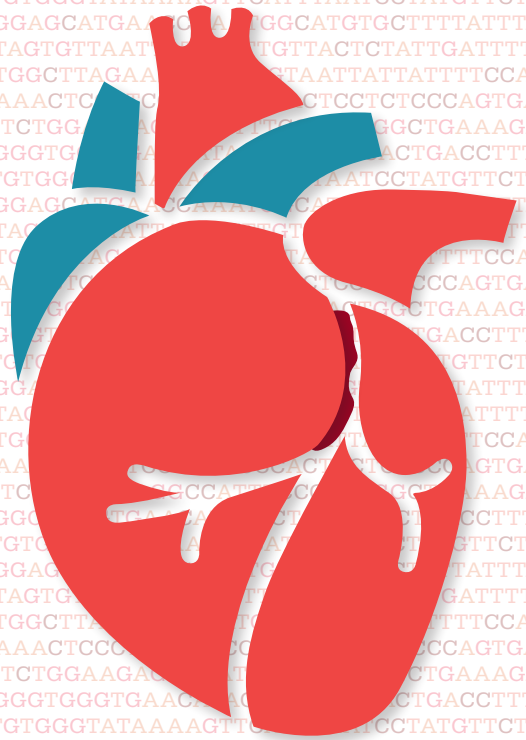
Implementing pharmacogenetics to personalize antiplatelet therapy after myocardial infarction

Impact section



Relevance

Cardiovascular diseases remain the leading cause of death worldwide and can significantly reduce quality of life and economic output. In the Netherlands, more than 34 thousand people are diagnosed with myocardial infarction each year. It has been well established that in these patients, antiplatelet treatment with the $P2Y_{12}$ inhibitors ticagrelor, prasugrel or clopidogrel helps to prevent life threatening events like myocardial infarction, stent thrombosis and stroke. Unfortunately, this comes at the cost of increased bleeding complication rates. These occur in up to 30% (depending on the selected population) of the patients in the year after myocardial infarction and require medical attention. Therefore, it is important to reduce the amount of bleeding complications in order to improve quality of life, reduce healthcare costs and reduce overall mortality. Clopidogrel does not reach its optimal effect in approximately 30% of the population, which is mostly caused by mutations in the *CYP2C19* gene that encodes the eponymous enzyme. Patients treated with clopidogrel and carrying these loss-of-function mutations experience more atherothrombotic events, while the other $P2Y_{12}$ inhibitors lead to more bleeding complications. Therefore, this thesis aimed to investigate whether using *CYP2C19* genetic testing to guide antiplatelet therapy could improve patient outcomes by reducing bleeding complication rates without increasing atherothrombotic event rates like myocardial infarction, stroke and death.

Target groups

The results of this thesis are of interest to clinicians who are directly involved in the treatment of patients who have had an acute myocardial infarction. Primarily, this is the case with cardiologists who are responsible for implementing the strategy in clinical practice, but also for primary care physicians and specialists like surgeons who might have to treat bleeding complications that occur during treatment with $P2Y_{12}$ inhibitors. Furthermore, clopidogrel is used frequently by neurologists as well and *CYP2C19* genetic testing is of increasing interest in patients with stroke, especially in patients with recurrent strokes while being treated with clopidogrel. Results of this thesis could help to start new prospective trials to investigate whether *CYP2C19* genetic testing could improve outcomes in stroke patients as well. This thesis is also of interest to health insurance companies and policy makers since a genotype-guided strategy could help to reduce healthcare costs while improving patient outcomes and quality of life.

Implication and implementation

A *CYP2C19* genotype-guided strategy resulted in fewer bleedings without an increase in events like myocardial infarction, stroke and death. These findings were published in the New England Journal of Medicine, which is one of the most impactful medical journals worldwide. It already has been cited in dozens of publications in the short period since its publication and has led to the genotype-guided strategy receiving a recommendation in the latest European Society of Cardiology guideline. This demonstrates the major impact of the trial and the interest for this topic of cardiologists and researchers worldwide. Many are interested in, or have already implemented the strategy in clinical practice. However, it is crucial that health insurance companies or governments reimburse the costs of the genetic test. The health economic analysis of the POPular Genetics demonstrated that a genotype-guided strategy results in improved quality of life, while reducing healthcare costs. Therefore, since in the Netherlands some hospitals have already implemented the strategy, insurance companies and governments are currently the ones saving costs, while hospitals face higher costs with buying the genetic tests. To ensure a broad implementation of the strategy in clinical practice, health insurance companies should cover these costs.