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### Oral antithrombotics and dentistry: Current state of affairs and guideline proposal

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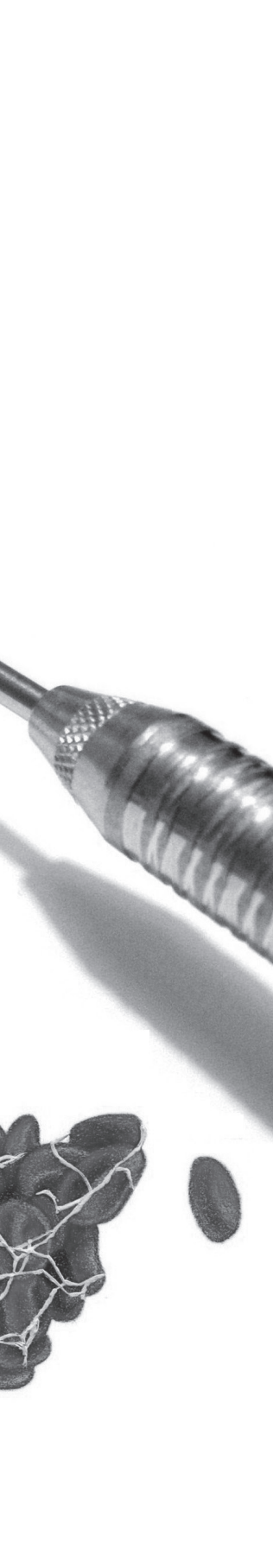
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# Chapter 1

## General introduction and aim of the study





In the Netherlands more people reach middle age while in the possession of their own natural teeth than decades ago. The percentage of completely edentulous people has decreased from 30% in 1981 until 10% in 2006<sup>1</sup>. Unfortunately, with increasing age, the chance of developing a chronic medical condition rises and medically complex patients are a growing part of the dental population<sup>2</sup>. The second most frequent chronic diseases in the Western World are cardiovascular disorders, such as myocardial infarction, stroke or deep venous thrombosis<sup>2</sup>. Since these disorders are in part caused by enhanced arterial or venous thrombosis, oral antithrombotic medication (OAM) is one of the mainstays of treatment protocols in patients with cardiovascular diseases. OAM can be divided into two, and since recently three, different groups of medications:

1. Thrombocyte inhibiting medication, like acetylsalicylic acid (ASA)(Aspirin<sup>®</sup>), carbasalate calcium (Ascal<sup>®</sup>), dipyridamol (Persantin<sup>®</sup>) and clopidogrel (Plavix<sup>®</sup>) mainly used to prevent arterial thrombosis, as in myocardial infarction and strokes;
2. Vitamin K antagonists (VKA), like warfarin, acenocoumarol and fenprocoumon (Marcoumar<sup>®</sup>), which are used in patients with atrial fibrillation, deep venous thrombosis, pulmonary emboli and in patients with mechanical heart valves;
3. The recently introduced “new oral anticoagulants” (NOAC), such as direct thrombin inhibitors dabigatran (Pradaxa<sup>®</sup>) and direct inhibitors of activated clotting factor Xa, such as rivaroxaban (Xarelto<sup>®</sup>) and apixaban (Eliquis<sup>®</sup>).

The duration of the treatment with OAM depends of the medical indication, and varies from 3 months until lifelong. The effect of these medications is to influence the blood clotting system in such a way that occurrence or recurrence of thrombosis will be prevented. Large studies have shown the beneficial effect of antithrombotic medication on the primary and secondary prevention of cardiovascular events<sup>3-6</sup>.

The side-effect of antithrombotic medication, however, is that it causes a bleeding tendency, which might be a problem in invasive dental treatment. Dentists and

oral and maxillofacial surgeons have been struggling with this double-edged sword for several years: do the OAM needs to be discontinued prior to invasive dental treatment to prevent serious bleeding complications? Until recently the standard procedure in patients using OAM has been to stop taking aspirin 7-10 days prior to dental treatment and to adjust the dose of VKA below an International Normalized Ratio (INR) of 1.8<sup>7</sup>.

Since 1997 several publications appeared in dental journals, discussing the aforementioned management and pointing to upcoming evidence that stopping the OAM might be more harmful to patients, exposing them to higher risks of (recurrent) thrombosis<sup>8-13</sup>. No clinical practice guidelines were available at that time.

The foregoing led to the present research project which is crystallized into this thesis with the following aims:

1. To study the dental literature on the effects of continuation of OAM on bleeding complications in dental patients undergoing invasive dental treatment and the effects of discontinuation of OAM on thrombotic complications;
2. To study the opinions and current management of Dutch dentists and oral and maxillofacial surgeons on invasive treatment in patients using OAM;
3. To formulate recommendations for an evidence-based clinical practice guideline for dentists on the dental management of patients using OAM during invasive dental treatment.

In **chapter 2** we describe the situation in 2008 in the Netherlands with regard to guidelines for the dental management of patients using OAM, based on what was known at that time. In **chapter 3** a systematic search for evidence-based clinical practice guidelines is performed and the subsequent critical evaluation with the AGREE instrument of these guidelines is pictured. **Chapter 4** contains a systematic review of studies that compare bleeding complications of invasive dental treatments in patients using either single or dual antiplatelet medication. In **chapter 5** we questioned Dutch dentists on topics related to invasive dental treatment in patients

using OAM and the management strategies they follow in treating these patients. **Chapter 6** describes a survey that was subsequently performed in Dutch oral and maxillofacial surgeons, on their management strategies in patients using OAM. In **chapter 7** we updated the evidence of clinical studies and existing clinical practice guidelines on the topic and used this to formulate a proposal for a Dutch clinical practice guideline. **Chapter 8** is designated for the general discussion, and **chapter 9** summarizes the findings and the conclusions from the research described in this thesis.

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